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THE AMERICAN JOURNAL OF ROENTGENOLOGY
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# INVESTIGATIONS INTO THE FIRST EFFECTS OF ROENTGEN RAYS ON LIVING PROTOPLASM AS STUDIED WITH MODERN FLUOROCHROMES

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## INTRODUCTION

THE understanding of the macroscopically observed effects in total body irradiation studies, in protection studies and organ shielding experiments requires detailed studies of the immediate effects of irradiation on single cells and small cell groups.

The first step in this direction was the work on micro-irradiation of *Amphiuma* blood cells by Buchsbaum and Zirkle.[3] The advantage of using plant cells became evident from the fundamental work of Herčik,[8] Biebl,[1] Petrová,[14] and Zirkle.[22] These investigators studied the irradiation effects appearing at relatively long time intervals after irradiation. Changes in the cell and its parts immediately after irradiation and during irradiation were not stressed in their investigations.

In the present work, the effects of roentgen rays on plant cells immediately after and during irradiation were studied with modern techniques and photographically recorded.

## EXPERIMENTAL

*A. Apparatus and Methods.* The material used for the observations was the isolated epidermis of *Allium cepa.* Under the conditions normally used (third onion shell, pieces of about 5 by 5 mm., different onion strains) the epidermis was suctioned gently from the mesophyll by the method of Strugger,[17] carefully removed with forceps and floated on tap water to await the particular experimental procedure.

The tissues were floated in a droplet of the selected solution onto a clear slide and were irradiated with 50 kv. (peak) roentgen rays from an AEG-50-T thin beryllium window tube (operated with 15 ma., without additional filter and at a target distance of 3.8 cm.). The dose was determined by the exposure time, which was varied from several seconds to ten minutes. According to the measurements of Rogers,[16] recent investigations of Jennings,[11] special measurements with nylon Victoreen thimble chambers and consideration of the corrections necessary, the radiation intensity under the above given conditions was about 120,000 roentgens per minute in air.

The tissues were studied by various techniques immediately after the irradiation: a fluorescence microscope, phase contrast equipment, dark field equipment and a bright field microscope. The fluorescence microscopical equipment consisted of a standard microscope (Bausch and Lomb), a light source with a blue filter (6 ampere carbon arc with blue filter Schott BG-3-BG-12 or Corning blue filter No. 5113), a cooling cuvette (5 per cent $CuSO_4$-solution, 3 cm. thick) and an eye protective

filter (Reichert yellow No. 3007 or Corning yellow No. 3486). The stains used were the fluorochromes acridine orange, auramine, and sodium fluorescein and the vital stain neutral red.

Particular attention was devoted to acridine orange because of its special properties and the advantages this stain offered in comparison with other vital stains. Two sources of acridine orange were used with the same results: acridine orange, National Aniline Division, C. I. 788 and acridine orange Bayer, Leverkusen.

The different stains were applied in appropriate concentrations, pH ranges and staining times according to the desired aims of the investigation. The stained sections were washed and studied in supporting solutions of the same nature. The pH was adjusted according to the table given by Strugger[17] by using proper amounts of the following standard solutions: 1/10 N HCl, 1/15 N monobasic potassium phosphate and 1/15 N dibasic sodium phosphate. Depending on the studies to be done, the sections were stained immediately after the irradiation (post-stained), before the irradiation (pre-stained) or at different time intervals after the irradiation (delayed-stained).

Special plasmolysis experiments with glucose and $KNO_3$ solutions were performed in order to study details of the irradiation effect and to localize the produced damage.

The photomicrographs were taken with the Leitz Micro Ibso attachment and a Leica housing. Both daylight and artificial light Kodachrome proved satisfactory.

*B. Results.*

1. Influence of Dose and Time. The irradiated sections were stained, together with controls, for five minutes in: acridine orange 1:5,000 in tap water at pH 7.94; auramine 1:10,000 in phosphate buffer at pH 5.45; sodium fluorescein 1:10,000 in phosphate buffer at pH 2.7; neutral red 1:2,000 in tap water at pH 7.2.

With acridine orange, auramine and neutral red the first effects immediately after the irradiation became manifest in the form of sharp dashes ("spots") on the side walls of single cells. They were characterized by a granular, flaky structure in the damaged areas and often by a marked warping of the cell wall. Their number and size depended upon the dose. With increasing dose of radiation, the effects became more numerous and extensive. With auramine and neutral red, the spots appeared in the same manner as with acridine orange. With sodium fluorescein, a very strong staining of the microsomes and chondriosomes could be observed immediately after irradiation while the spot phenomenon did not appear to be as pronounced (see Fig. 1–16). The results are shown in detail in Tables I, II, III and IV.

Sections pre-stained for five minutes in acridine orange (1:5,000 in tap water at pH 7.94) were irradiated for five minutes in an acridine orange droplet and observed immediately after the irradiation. The spots had the same appearance and arrangement as in the post-stained samples, indicating that the "first effects" occurred during the irradiation. Sections pre-

→

FIG. 1. Onion epidermis, control. Acridine orange 1:5,000, pH 10.5; five minutes stain. Homogeneous picture, all cells alive.

FIG. 2. Onion epidermis, two minutes irradiation. Acridine orange 1:5,000, pH 10.5; five minutes stain. Cells alive, only one cell shows the characteristic first effect; small red fluorescing dash ("spot").

FIG. 3. Onion epidermis, four minutes irradiation. Acridine orange 1:5,000, pH 10.5; five minutes stain. Number of spots increased.

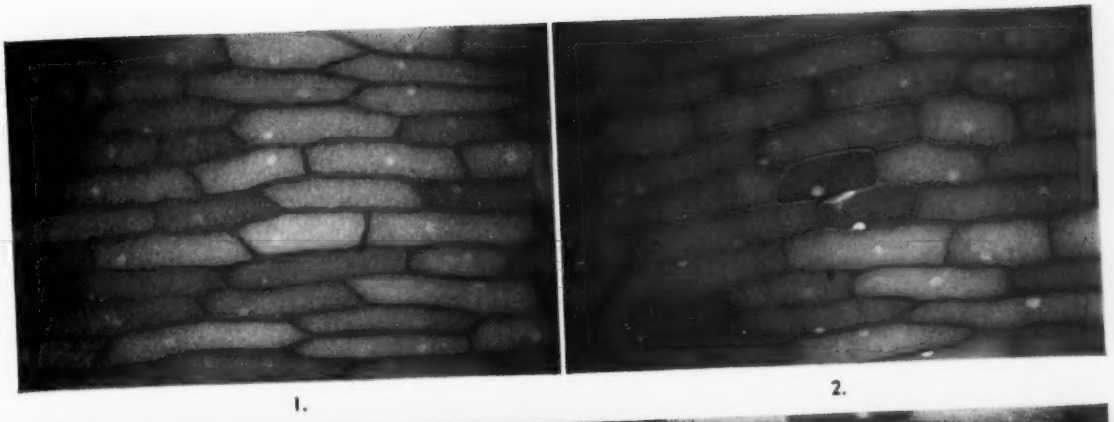
FIG. 4. Onion epidermis, six minutes irradiation. Acridine orange 1:5,000, pH 10.5; five minutes stain. Spots very numerous, coagulation in the spot area, warping of the cell wall, changes in nuclei.

FIG. 5. Onion epidermis, eight minutes irradiation. Acridine orange 1:5,000, pH 10.5; five minutes stain. Increased number of spots, larger areas involved, strong deformation of cytoplasm and cell wall.

FIG. 6. Onion epidermis, lethal irradiation. Acridine orange 1:5,000, pH 10.5; five minutes stain. Completely killed preparation, entire protoplast red fluorescing.

FIG. 7. Onion epidermis, control. Acridine orange 1:5,000, pH 7.5; five minutes stain. Homogeneous picture, all cells alive.

FIG. 8. Onion epidermis, ten minutes irradiation through small hole in lead shield (diameter about 0.5 mm.). Acridine orange 1:5,000, pH 7.5; five minutes stain. Red fluorescence of the irradiated cells in the diaphragm area, normal appearance of the lead shielded, unirradiated cells.



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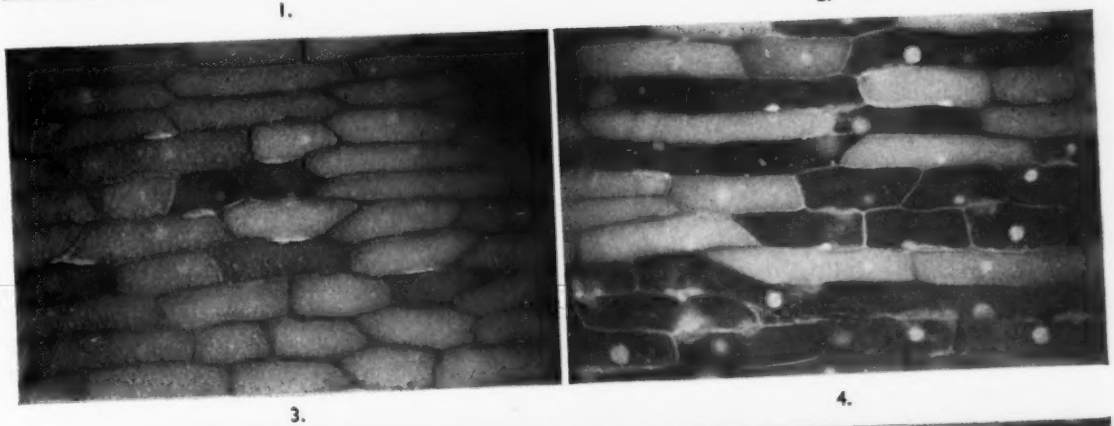

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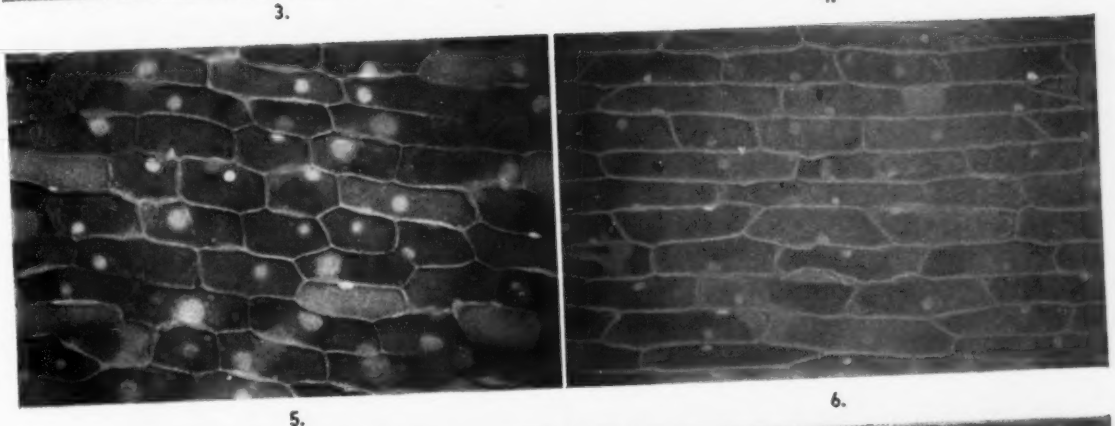

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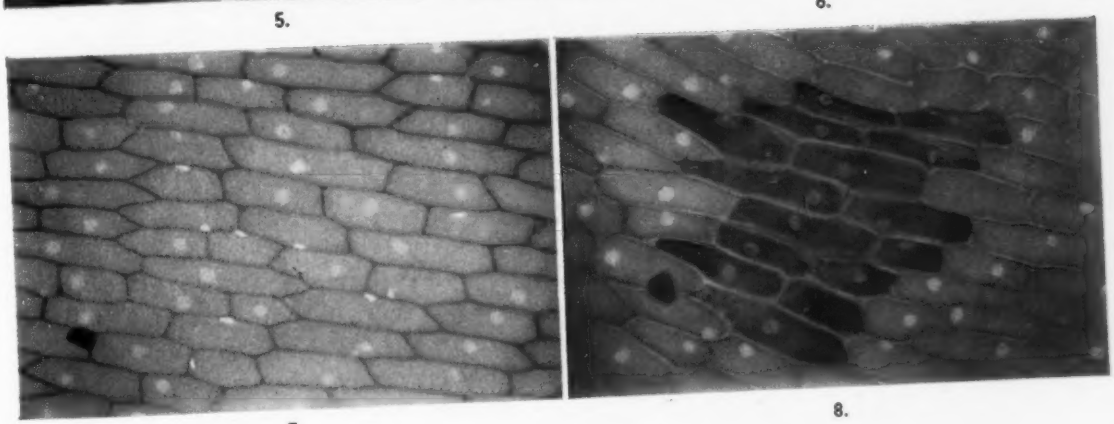

7. 8.

TABLE I

ACRIDINE ORANGE

(See Fig. 1–8)

| Preparation | Histological Description |
|---|---|
| Control, non-irradiated | Normal, homogeneous picture. Cell walls, pale green; cytoplasm, dark green; nuclei, bright green; vacuoles, slightly reddish yellow (see Fig. 1) |
| 2 minutes irradiation | Single bright red fluorescing spot appeared in only one cell (see Fig. 2) |
| 4 minutes irradiation | Number of spots increased (see Fig. 3) |
| 6 minutes irradiation | Number of spots quite numerous; many cell walls appeared warped; many of the nuclei in or near the spot areas were influenced (see Fig. 4) |
| 8 minutes irradiation | Spot phenomenon markedly increased; larger area affected (see Fig. 5) |
| 10 minutes irradiation | All cells red and fluorescing, indicating complete non-viability (see Fig. 6) |

stained with auramine also showed, directly after irradiation, the characteristic spot phenomenon with structural changes of the cytoplasm in the spot area and warping of the cell walls.

Epidermis sections were irradiated for five minutes and then floated in tap water. At different time intervals after the irradiation they were stained in the above mentioned acridine orange or auramine solutions. Depending on the time interval between irradiation and staining, latent effects became manifest in the form of a more or less marked spreading of the damage from the spot area throughout the cell and into adjacent cells. With increasing time this spreading damage became more manifest so that by two hours after irradiation there was not only a change in the fluorescence color but also in the structure, the protoplast appearing more or less granular and flaky.

2. Influence of pH. Because of the extreme importance of the pH of the supporting solutions, both in staining and in irradiation, the spot phenomenon was studied under a wide range of pH values. These included: acridine orange experiments at pH values 2.3 to 11.3; auramine experiments at pH values 2.6 to 11.1; sodium fluorescein experiments at pH values 2.3 to 6.7; neutral red experiments at pH values 3.8 to 9.2.

a. Acridine orange experiments: All sections were irradiated under identical conditions

TABLE II

AURAMINE

(See Fig. 9–12)

| Preparation | Histological Description |
|---|---|
| Control non-irradiated | Normal, homogeneous picture. Cell walls, pale green; cytoplasm, weak yellow; nuclei, yellow green |
| 2 minutes irradiation | An occasional single cell showed a bright golden fluorescing spot |
| 3 minutes irradiation | Spots more frequent. Granular, flocculated appearance in spot areas |
| 4 minutes irradiation | Spots appeared more pronounced |
| 5 minutes irradiation | Spots more numerous. Many nuclei in vicinity of spots fluoresced brightly |
| 10 minutes irradiation | Entire protoplasm fluoresced. Nuclei were bright and cytoplasm granular and flaky |

TABLE III

SODIUM FLUORESCEIN

(See Fig. 13 and 14)

| Preparation | Histological Description |
|---|---|
| Control non-irradiated | Cell walls unstained; cytoplasm, green. Numerous plasma strands that fluoresced strongly. The microsomes and chondriosomes showed a weak fluorescence |
| 5 minutes irradiation | Cell walls appeared dark; cytoplasm, green. Plasma strands were not evident and the microsomes and chondriosomes fluoresced brightly. Spots that were present were practically invisible |

and stained for five minutes in acridine orange 1:5,000 prepared with phosphate buffers. The spots appeared with a pH of 2.94. They became more and more brilliant with increasing pH, the optimal fluorescence being in the pH range of 7.5 to 8.8. It should be emphasized and may be seen from Table v that the occurrence of the radiation effect is independent of the pH value in the range of 2.9 to 11.3. The characteristic first effects in the form of spots occurred at all pH values in the given range, but their appearance as to the color and brightness of fluorescence differed. With the higher pH values the characteristic red fluorescence became brighter.

b. Auramine experiments: All sections were irradiated under identical conditions and stained for five minutes in auramine 1:10,000 with phosphate buffers. The spots stained faintly with a pH of 3.49. Fluorescence increased with rising pH and could be seen best in the pH range of 7.3 to 8.5.

c. Sodium fluorescein experiments (1:10,000 with phosphate buffers, stained five minutes): Spots were not revealed in the pH range of 2.34 to 6.68. In this range, however, the microsomes and chondriosomes stained with a bright golden yellow fluorescence after the irradiation. In several cells the fluorescence was absent, an effect observed by Herčik at longer time intervals after irradiation. They appeared dark on a bright background.

d. Neutral red experiments: With neutral red solution the spots could be distinguished from the red stained cell walls by the change in the structure of the cytoplasm and especially the deformation of the cell wall. With increasing pH values the spots became more visible; they were most easily observed in the pH range of 7.6 to 8.0. With a pH of 9.15 (neutral red base solution) the spots were a bright cherry red color.

To obtain more information concerning the staining mechanism of neutral red base, acidification and realkalinization experiments were performed. For this purpose epidermis sections, irradiated for five minutes, were stained for five minutes in a neutral red solution, 1:2,000 in tap water at pH 7.2. Using the bright field microscope, numerous spots with a bright cherry red color were observed. Cells without focal areas of damage exhibited a normal appearance, particularly the homogeneous staining of the vacuoles. The preparation was then, while under the microscope, treated with 1/50 N NaOH. As soon as the alkaline solution, which was added from the side, reached the spot cells the cherry red color of the spots faded to a yellowish color and at the same time needle shaped crys-

TABLE IV

NEUTRAL RED

(See Fig. 15 and 16)

| Preparation | Histological Description |
|---|---|
| Control non-irradiated | Homogeneous appearance. Cell walls, cytoplasm and nuclei were unstained. The vacuoles stained red |
| 5 minutes irradiation | Spots stained red. Cytoplasm in spots appeared granular and flocculated. Cell walls appeared bulged. Nuclei in the spot area stained red; other nuclei were invisible. Cell sap appeared damaged and was colorless |

Table V

ACRIDINE ORANGE EXPERIMENTS

Influence of pH on Staining Reaction

| pH | Cell Wall | Cytoplasm | Nucleus | Vacuole | Spots |
|---|---|---|---|---|---|
| 2.32 | Green | Green | Weak | Unstained | Unstained |
| 2.94 | Weak red | Green | Weak | Unstained | Weak yellowish |
| 3.81 | Red | Green | Weak | Unstained | Weak orange-pink |
| 4.99 | Red | Green | Weak | Unstained | Red |
| 6.12 | Red | Green | Weak | Unstained | Red |
| 6.51 | Red | Dark green | Weak | Unstained | Red |
| 7.09 | Orange red | Green | Green | Reddish | Strong red |
| 7.68 | Green | Green | Green | Reddish | Very bright red |
| 8.71 | Green | Green | Green | Reddish | Very bright red |
| 11.27 | Weak green | Green | Green | Reddish | Bright glittering red |

tals grew into the cell from the spot area. When, while still under the microscope, the preparation was reacidified by adding phosphate buffer (pH 4.9) from the side, the crystals in the spot cells dissolved and the spots reappeared in their earlier cherry red color (see Fig. 17–19). In the spot free cells the dye also was precipitated by the alkalinization but in contrast to the needle-like crystal formation in the spot cells the dye was precipitated in the form of randomly distributed small irregular crystals (Fig. 20 and 21).

3. Plasmolysis Experiments. To prove that the observed spot effect was in fact an irradiation effect on the living protoplasm and not on the cell wall, experiments were performed in which either plasmolyzed cells were irradiated or in which irradiated cells were plasmolyzed.

Cells were plasmolyzed for periods up to two hours in a 1 molar glucose solution (prepared with tap water), then irradiated for six minutes and stained in acridine orange (1:5,000 1 molar glucose, pH 7.41). No damage to the cell walls was apparent. The spots occurred in the plasmolyzed cytoplasm fluorescing a bright glittering red (see Fig. 22–24).

Cells irradiated for six minutes, stained and then plasmolyzed in a 1 molar $KNO_3$ solution also revealed the spots as damaged areas in the plasmolyzed layers. Staining experiments with auramine confirmed these findings.

In general, the spot-bearing cells showed three kinds of plasmolysis: Cells with small spots plasmolyzed much faster than spot-free cells, generally showing cap plasmolysis; cells with larger spots preferably plasmolyzed in tonoplast plasmolysis; cells with very large spots very rarely plasmolyzed, indicating that their ability to plasmolyze was seriously interfered with by the irradiation.

4. Dark Field Microscopical Investigations. Under the dark field microscope unirradiated controls presented the normal picture described by Strugger.[17] The individual microsomes were bright and with them plasma streaming with its characteristic activity could be recognized. The normal living cytoplasm appeared dark. Brownian movement was very marked.

In the irradiated sections the spot cells were recognized by local deformation of the longitudinal cell walls. The cytoplasm in these areas had completely lost its optical homogeneity. The silvery micromeres formed an area of agglutination which stood out from the surrounding cytoplasm. No plasma streaming and no brownian movement could be seen in the spots and had ceased or was greatly retarded in other cell areas of the irradiated sections.

5. Bright Field and Phase Contrast Microscopical Investigations. The normal unirradiated cells showed all the cytological details found by Strugger[17] in 1947. In the irradiated sections the spots could be recognized by the local deformation of the cell membrane and by the granular structure of the cytoplasm. The absence of brownian movement in the spot areas, in comparison with the strong molecular movement outside of the spots, was an outstanding characteristic.

Detailed phase contrast investigations under high power clearly showed the deformation of the cell wall and the granular area with irregular edges in the spot area. The cytoplasm in the spots was refractile and exhibited a strong brilliance. The chondriosomes in the spots were rounded and an extensive vacuolization ap-

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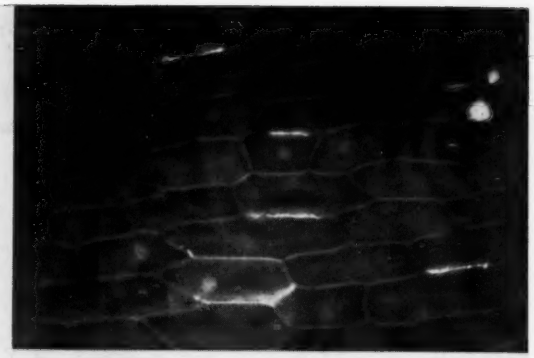

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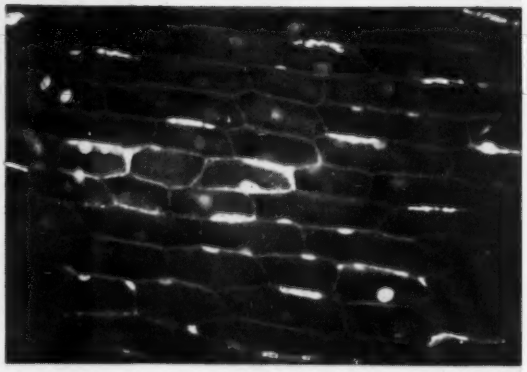

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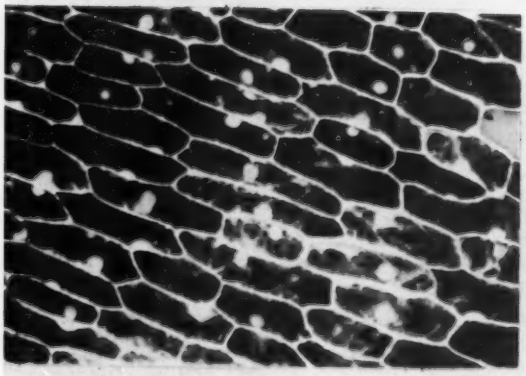

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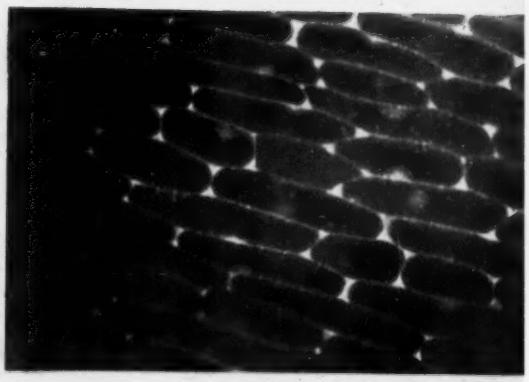

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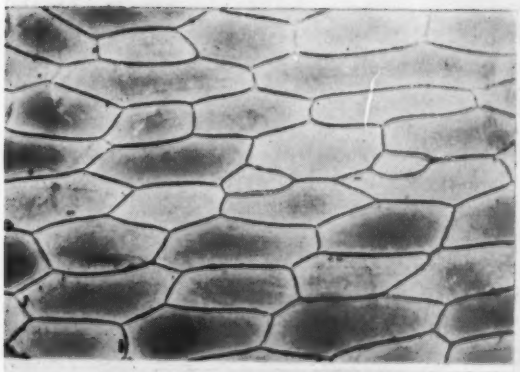

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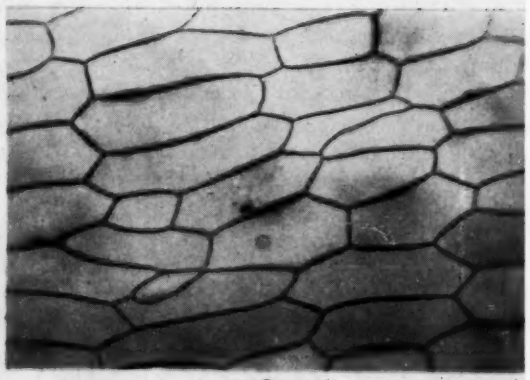

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peared in the coagulated cytoplasm of the spot areas. No cytoplasmic streaming and no brownian movement could be detected.

If the nucleus was located in the spot area it showed a definite and marked change in its structure as compared with nuclei located outside the spot area. Its inner structure appeared as an irregular pattern, with chromomeres fixed in granular areas while the chromomeres of normal nuclei showed the usual arrangement.

## DISCUSSION

The use of modern fluorochromes, especially acridine orange, for viability studies on metaphyte cells and thallophyte cells was systematically investigated by Strugger and his associates.[17] They found that under special experimental conditions (proper stain concentration, pH values and staining times) the differentiation between viable and non-viable tissue was possible, due to the "concentration effect" this fluorochrome exhibits. In general, living protoplasm takes up small amounts of the stain and shows a green fluorescence while damaged protoplasm takes up larger amounts and shows an orange to red fluorescence depending upon the degree of destruction.[17] This color change holds true for heat damage, chemical damage and mechanical injury.

Radiation damage was studied for the first time with this method in 1943 by Krebs[12] and later by Krebs and Gierlach,[13] who investigated the irradiation effects of alpha rays on onion epidermis and yeast cells during the irradiation and immediately after the irradiation.

The present investigations have shown that the method also can be applied to the study of roentgen-ray effects on protoplasm. The first effects or the early effects on the protoplasm of living onion epidermis cells appeared in the form of well defined strongly localized red stained areas ("spots") in the cytoplasmic layers of the cells. The frequency of the spots depended on the irradiation dose—higher doses increasing the number and size of the spots. They appeared in most cases along the longitudinal side walls of the cell and only occasionally on the end cross walls. The cell wall showed a characteristic deformation and warping while the red stained cytoplasm in the spot area showed a granulated or flocculated structure without any infringement on the edges of the green fluorescing normal living protoplasm. Under the given experimental conditions the first effects always occurred in the cytoplasm. The nucleus was involved in the effect only when it was located in or close to the spot area. In such cases it presented a color change from green to yellow-orange or red. If the nucleus was located outside the spot area it always presented a normal appearance and a green fluorescence.

These characteristic first effects occurred during the irradiation. At longer time inter-

FIG. 9. Onion epidermis, two minutes irradiation. Auramine 1:10,000, pH 5.51; five minutes stain. Characteristic initial effect on one cell.

FIG. 10. Onion epidermis, three minutes irradiation. Auramine 1:10,000, pH 5.51; five minutes stain. Areas of effects increased, local damage to cytoplasm.

FIG. 11. Onion epidermis, four minutes irradiation. Auramine 1:10,000, pH 5.51; five minutes stain. Numerous spots, coagulation of the cytoplasm, nuclei located in or near a spot show fluorescence.

FIG. 12. Onion epidermis, six minutes irradiation. Auramine 1:10,000, pH 5.51; five minutes stain. Number of spots markedly increased, coagulation of cytoplasm in spot areas, warping of the cell wall, some degree of nuclear damage.

FIG. 13. Onion epidermis, control. Sodium fluorescein 1:10,000, pH 2.7; two minutes stain. Plasma strands strongly fluorescing.

FIG. 14. Onion epidermis, five minutes irradiation. Sodium fluorescein 1:10,000, pH 2.6; two minutes stain. Plasma strands retarded, vacuoles contracted, strong fluorescence of the microsomes and chondriosomes.

FIG. 15. Onion epidermis, control. Neutral red 1:2,000, pH 7.2; five minutes stain. Homogeneous picture, uniform vacuole staining and cell wall staining.

FIG. 16. Onion epidermis, five minutes irradiation. Neutral red 1:2,000, pH 7.2; five minutes stain. Central spots red with red stained cell wall and red shining cytoplasm, warped cell walls.

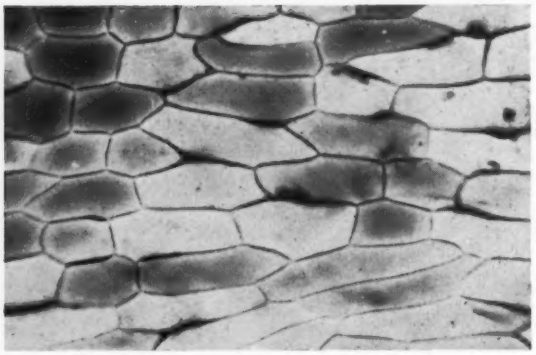

FIG. 17. Onion epidermis, five minutes irradiation. Neutral red 1:2,000, pH 7.5; five minutes stain. Numerous spots, coagulation of the spot cytoplasm, warping of cell wall.

vals between irradiation and observation, delayed effects occurred. In the delayed effects the damage spread from the spot areas over the whole cell and influenced adjacent cells. Herčik, in his onion epidermis alpha-ray experiments, observed such a spreading from damaged cells to undamaged adjacent cells. Since the washing of the irradiated sections for hours in tap water prevented the spreading, he concluded that toxic substances may be involved in the process,[9] an idea discussed frequently at the present time (Hevesy[10]).

There is a general belief that radiation damage is associated with an acidification in the irradiated tissue.[7] The acidification and re-alkalinization experiments with neutral red tend to favor this theory. Furthermore, the cytoplasm in the damaged areas must have undergone changes in its structure which favored and or caused the growing of oriented needle-like crystals.

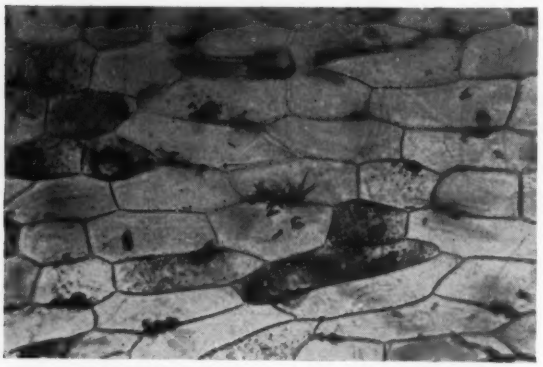

FIG. 18. Figure 17, alkalinized with 1/50 N NaOH, showing formation of needle crystals in spot cells, precipitation of randomly distributed small crystals in spot free cells.

The pH of the stain solution influences the brilliance of the fluorescence that is developed. The radiation effect occurs over a wide pH range and is independent of any specific pH in this range. This observation held for the experiments with acridine orange, as well as for the investigations with auramine and neutral red. Of special interest were the findings with sodium fluorescein, an acid stain. This fluorochrome has been used in radiobiological work by Herčik,[9] who studied the effects of alpha rays on onion epidermis two hours after irradiation. He distinguished four degrees of radiation damage, the most characteristic being a total absence of the fluorescence in totally killed cells. The present studies of the early changes confirm these findings. They reveal, moreover, that this stain, which is not able to illustrate the spot phenomenon, does produce a strong staining of the mitochondria and the microsomes immediately after irradiation.

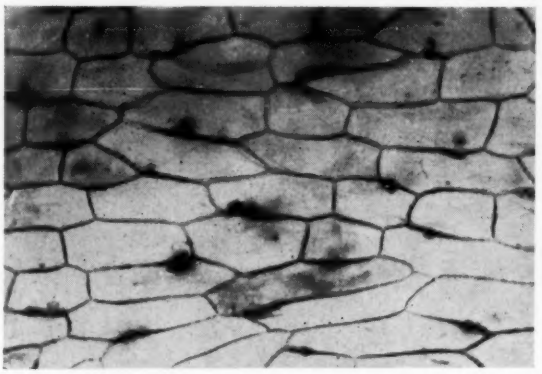

FIG. 19. Figure 18, reacidified with phosphate buffer, pH 4.91 with dissolving of the crystals and reappearance of the original spots.

The experiments done with plasmolyzed cells (cells plasmolyzed and then irradiated) and with irradiated cells (cells irradiated and then plasmolyzed) demonstrated that the effect is produced in the cytoplasm. Furthermore, they showed that the spot cells were a result of irradiation damage. Cells with spots always plasmolyzed faster

and in pathological forms (cap plasmolysis, tonoplast, plasmolysis) when compared with normal, spot free cells. In connection with the observations of Wanner[20] this indicates that permeability of spot bearing cells is altered by the irradiation. The damage to the cell could be marked enough (and this was the case in sections which showed totally red fluorescing protoplasm) for it to lose its plasmolysis ability. This fact, according to experience in cellular physiology, demonstrates the death of the total protoplast.

Microscopical investigations of irradiation damage confirmed the reported staining experiments. They revealed not only

Fig. 20. Onion epidermis, five minutes irradiation. Neutral red 1:2,000, pH 7.2; five minutes staining. Alkalinized with 1/50 N NaOH. Spot cells show needle crystals growing from the spot area into the cell; several cells show randomly distributed fine crystals; several cells appear undamaged.

morphological changes in the spot areas but also demonstrated functional changes in the damaged areas. The cytoplasm in the spots possessed the characteristic bright refractility for dead protoplasm. There was granular flocculation and vacuolization in the spot regions. Cytoplasmic streaming and brownian movement of the microsomes and chondriosomes was absent in the spot regions. The spot bearing cells, in general, showed a slowing of the plasmic streaming, a retraction of the plasma strands and a more or less pronounced vacuolar contraction. The form of the larger leukoplasts changed, with a tendency to round themselves and to enlarge their vac-

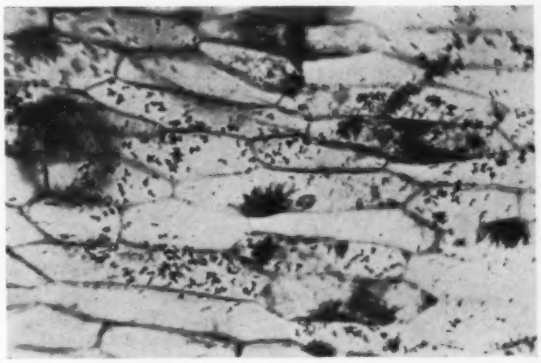

Fig. 21. Similar to Figure 20. Spot cells with focal crystallization; randomly distributed fine crystals in many other cells.

uoles. These findings confirmed and extended the experiments of Wanner[20] and of Bishop, McLaughlin and Tapley.[2]

Wanner studied the influence of roentgen rays (50 kv., peak, unfiltered radiation, 1,000 to 36,000 roentgens) on *Allium cepa* epidermis cells. He found, as initial effects of irradiation, a vacuolization of the cytoplasm which, depending on the dose, proved to be reversible within certain limits. Higher doses markedly influenced the chondriome. The changes consisted of a mycelioid-like growth and of changes in the form of the chondriosomes. The nucleus showed, even with the highest applied dose, only a slight roughening of its structure. From irradiation experiments in which the cytoplasm and nucleus were

Fig. 22. Onion epidermis, eighty minutes in 1 mol glucose, pH 5.82 plasmolyzed; five minutes irradiation; five minutes staining in auramine glucose 1:10,000, pH 5.51. Normal plasmolysis; in the middle of the picture one cell—one-half of which is heavily damaged, while the other half shows normal appearance.

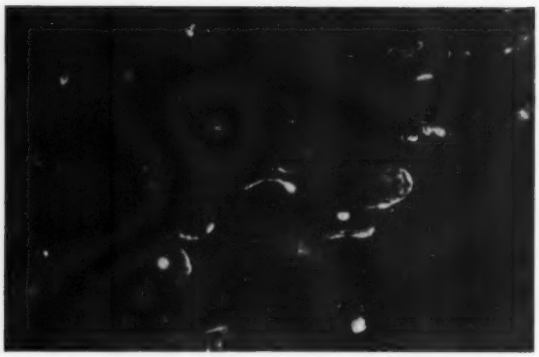

FIG. 23. Onion epidermis, eighty minutes in 1 mol glucose, pH 5.82 plasmolyzed; six minutes irradiation; five minutes staining in auramine glucose 1:10,000, pH 5.51. Irradiation damage in several cells; they show clearly that the initial effects are produced in the cytoplasmic layer.

separated by plasmolysis, Wanner concluded that the observed effects were direct effects on the cytoplasm and that their occurrence was not necessarily associated with effects on the nucleus. He also observed a slowing of the cytoplasmic streaming and a change in the refraction of the irradiated cytoplasm.

Bishop, McLaughlin and Tapley irradiated living cells of *Tradescantia paludosa* and *Tradescantia virginiana* with roentgen rays and used the rate of cytoplasmic streaming as an index of cellular viability. Seven hundred thousand roentgens (140 kv., 1 mm. Al, 1,200 r per minute) produced a complete cessation of all streaming in the cells.

The role played by the different cell parts in radiation effects is a widely discussed problem. Del Buono[4] showed that with medium doses the initial damage occurred in the cytoplasm, consisting in a swelling of the mitochondria, which was followed by fragmentation and later vacuolization. He also reported a conversion of the mitochondria into lipoid droplets. Investigations of the ovocytes of the irradiated ovaries of mice showed changes in the chondriosomes with dissolution of the mitochondria as initial effects. In irradiation experiments of cancer cells the damage to the chondriosomes of the Golgi net appeared two to seven days earlier than the damage to the nuclei. Del Buono concluded that the chondriosomes were the most sensitive elements of the irradiated cytoplasm. In this connection the findings of the present study with sodium fluorescein are of interest. With this stain, an effect immediately after irradiation became manifest in the microsomes and chondriosomes which stained with a bright yellow fluorescence.

Graul[6] believed that the initial effects following irradiation acted on chemical processes, which occurred in the cell boundary layers and that these changes contributed to the biological radiation effects in a manner as important as the way in which influences on the cell governing center (nucleus) determine the fate of the cell. The importance of this idea for the understanding of the observed initial effects and for protection studies is obvious, especially in connection with the theories developed by Failla,[5] Reynolds,[15] and Zirkle.[21]

## SUMMARY

The reported experiments with vital stains, supported and checked by other methods, demonstrated that modern fluorochromes, especially acridine orange, can be used in radiobiology for the detection of radiation damage. The method makes possible the detection of early radiation effects on protoplasm as well as the observation of

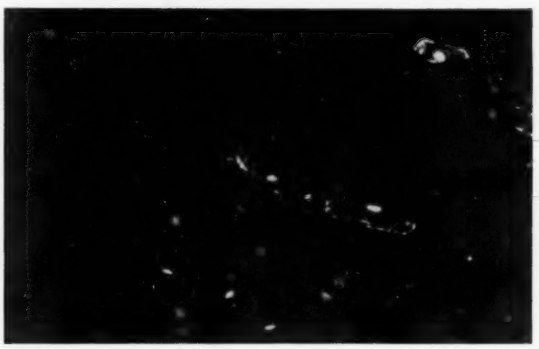

FIG. 24. Onion epidermis, 135 minutes plasmolyzed in 1 mol glucose, pH 5.82; six minutes irradiation; five minutes staining in auramine glucose 1:10,000, pH 5.51. Smaller and larger spots in the plasmolyzed protoplasts; two or three cells show damaged nuclei in addition to cytoplasmic damage.

delayed effects. *Allium cepa* epidermis, irradiated with adequate doses of roentgen rays to produce damage (120,000 to 800,000 r), then immediately stained, showed the initial effects in the form of damaged areas ("spots") along the longitudinal walls of the cell. Investigations utilizing auramine and neutral red, the bright field microscope, dark field equipment, and phase contrast apparatus, as well as plasmolysis experiments, revealed these spot effects as partial destruction of smaller or larger cytoplasmic areas. Irradiated sections, stained at different time intervals after the irradiation, showed a spreading of the damage, demonstrating that delayed effects also could be detected and studied with the method. *Allium cepa* epidermis sections pre-stained with acridine orange and then irradiated, showed the effects during irradiation as was reported earlier for alpha rays by Krebs.[12] While Herčik's earliest observations were made two hours after beginning irradiation, the method reported here permitted observation of very early effects since the doses necessary could be applied in one to three minutes.

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# RECURRENCES AND METASTASES IN CANCER OF THE BREAST

## AN ANALYSIS OF ONE HUNDRED CASES*

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IT IS a well known fact that sooner or later after cancer of the breast has been treated, the disease may again manifest itself. Bone, visceral and skin metastases and recurrences often occur from any grade of breast cancer and are a manifestation of the generalized extension of the disease throughout the body.[13]

Recently, several patients with cancer of the breast seen in the Department of Radiology of the Hospital of the University of Pennsylvania have come to our attention because of a definite cyclic chronological pattern in the occurrence of their metastases and recurrences. The following case illustrates the type of "cyclic recurrence" of breast cancer observed in these patients.

### REPORT OF CASE

CASE 1 (No. 13070). F. E. H., a fifty-six year old white single female, was first seen in the Department of Radiology of the Hospital of the University of Pennsylvania on July 12, 1938, because of a 6 cm. ulceration involving the left breast and fixing it to the chest wall. The patient had been aware of the presence of an ulceration of her left breast for at least one and one-half years prior to her visit to the hospital. Our examination revealed palpable lymph nodes along the tail of the left breast, but roentgenograms of the chest and bones failed to reveal any evidence of metastatic disease. Treatment of the patient was begun with a course of deep and intermediate radiotherapy directed to the left breast and axilla. The local lesion responded well to this therapy so that the breast in time was no longer fixed to the chest wall.

A simple mastectomy was recommended and was carried out by Dr. I. S. Ravdin on November 22, 1938.

The patient was followed up with no evidence of disease until April 5, 1940, when a recurrence was noted in the left axilla (three years after the onset of the disease). This was excised surgically and revealed cancer.

The patient continued to do well with no evidence of recurrence until March 17, 1943, when two "lumps" were noted on the left anterior chest wall (six years after the onset of the disease). These nodules were excised surgically on April 3, 1943. Soon thereafter, metastatic nodules beneath the left clavicle and in the left anterior axillary fold were discovered and were treated with radium needles, with disappearance of the lesions.

The patient again remained free of disease until June 9, 1944 (seven years after the onset of the disease), when a recurrence was noted in the mid-portion of the old surgical scar. This was treated with radium with good results. Beginning in November, 1944, multiple skin nodules appeared on the anterior chest wall. These were treated with intermediate and superficial radiotherapy with an initial good response, but with a gradually decreasing effect.

In November, 1945 (eight years after the onset of the disease), the patient developed metastases to the ribs and lungs and was given open field radiotherapy to the chest with some improvement in her cough.

After 1945 the patient was not seen again in the Department of Radiology, but she was contacted periodically by the Tumor Follow-up Clinic. She died on February 12, 1948, approximately eleven years following the onset of the disease.

The present study was undertaken in an attempt to determine whether the tendency towards a cyclic type of recurrence in cancer of the breast, as observed in the foregoing case, occurred with any degree of regularity in a group of unselected cases of cancer of the breast. In order to be assured that the cases selected would have adequate

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follow-up data, the cases were selected from the "Dead File" of the Department of Radiology. Using the standard statistical method for random sampling by means of "Tippett's numbers," 100 cases out of an approximate 450 cases of patients with cancer of the breast, who had been seen in the Department of Radiology since 1930 and who had subsequently died, were selected. Due to incorrect filing, the report of a patient who is still alive was included with the 100 selected cases. However, the follow-up period has been sufficiently long (more than fifteen years) to justify the inclusion of this case for certain of the statistical analyses.

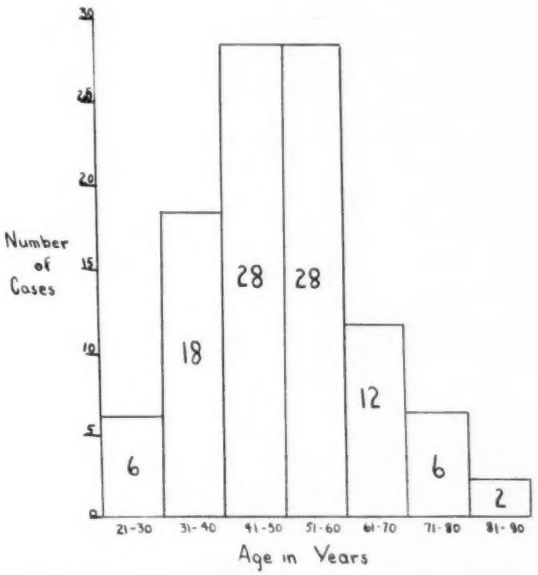


FIG. 1*A*. Age distribution in 100 cases of cancer of the breast. (Age of patients at time first seen in Department of Radiology.)

Figure 1*A* indicates the age distribution in this series of 100 patients at the time they were first seen in the Department of Radiology of the Hospital of the University of Pennsylvania. Figure 1*B* indicates the age distribution in the series corrected so that the age corresponds to the estimated time of onset of the disease in the patient. From both of these curves it is clear that the peak age incidence was in the forty to fifty year decade. This agrees with the usually quoted age distribution in this disease.[2,5,14]

Table 1 indicates the type of therapy employed in this group of 100 patients. More than three-fourths (76 per cent) of the patients had a combination of surgery and roentgen therapy. Fifteen per cent had roentgen therapy alone, 6 per cent had surgery alone, and 3 per cent had no therapy of any kind. Table 1 also includes the arithmetic mean number of years between the estimated onset of the disease and the death of the patient for the various therapeutic groups. It is interesting to note that there is no difference in survival for the various groups, with the exception of the group that had surgery alone, which latter shows a slightly longer survival rate. Since, however, this group included only 6 cases, this difference is not statistically significant. This apparent increase in survival in this group may be due to the fact that 4 of these 6 patients had radical mastectomies within a few months after

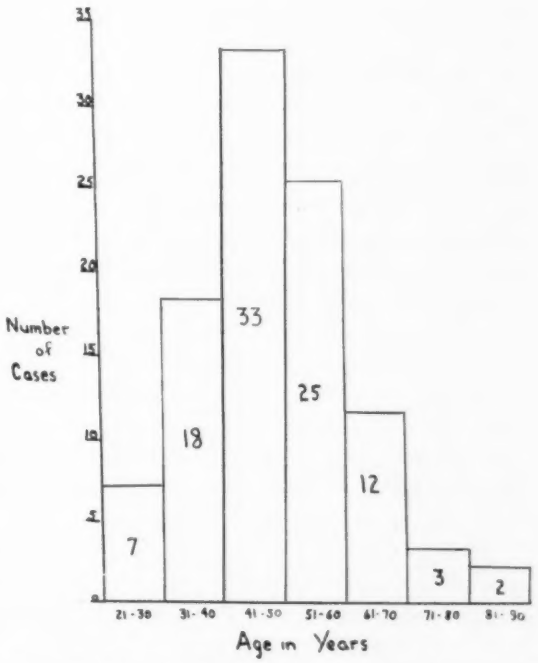


FIG. 1*B*. Age distribution in 100 cases of cancer of the breast. (Age of patients at time of estimated onset of disease.)

TABLE I

TYPE OF THERAPY EMPLOYED AND AVERAGE SURVIVAL

| Number of Cases | Type of Therapy | Arithmetic Mean Number of Years Between Estimated Onset of Disease and Death |
|---|---|---|
| | | years |
| 3 | None | 3–4 |
| 15 | Roentgen therapy alone | 3–4 |
| 6 | Surgery alone<br>5 radical mastectomies<br>1 simple mastectomy | 4–5 |
| 76 | Surgery plus roentgen therapy<br>43 radical mastectomies<br>14 simple mastectomies<br>19 type of surgery not stated | 3–4 |
| Total 100 | | |

the estimated onset of the disease. This early definitive therapy may have been the chief contributing factor to the prolonged survival in this group if that increased survival actually represents a real difference as compared with the other groups. It should also be pointed out that the use of roentgen therapy plus surgery does not appear to increase the survival rate. Many of the patients in this group received postoperative irradiation directed to the operative field, as well as prophylactic irradiation directed over lymphatic drainage areas. These data agree with the conclusions arrived at in previous communications by Pendergrass *et al.*,[10,11,12] in which a total of 793 cases of cancer of the breast were reviewed and the opinion expressed that there was no evidence that postoperative irradiation had any favorable effect on the five year survival rate.

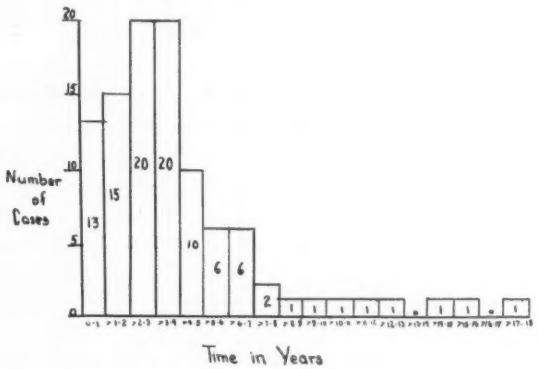


FIG. 2. Length of survival in years after estimated onset of disease. Arithmetic mean number of years between estimated onset of disease and death is three to four years for series.

In Figure 2, the survival in years after the estimated onset of the disease is indicated. The average survival in this whole group was three to four years. It must be remembered that these cases represent a heterogeneous group with respect to the type of therapy employed (see Table 1). It becomes difficult, therefore, to compare this survival rate with the survival rates in the literature which usually refer to the results of one specific therapeutic regimen. If, however, the survival rates for each therapeutic group as obtained from the literature[1,2,5,7,14,15] are averaged together in the ratio corresponding to the ratio of the number of cases in each therapeutic group to the total number of cases, the results obtained agree closely with those obtained in our group.

In order to tabulate data concerning the

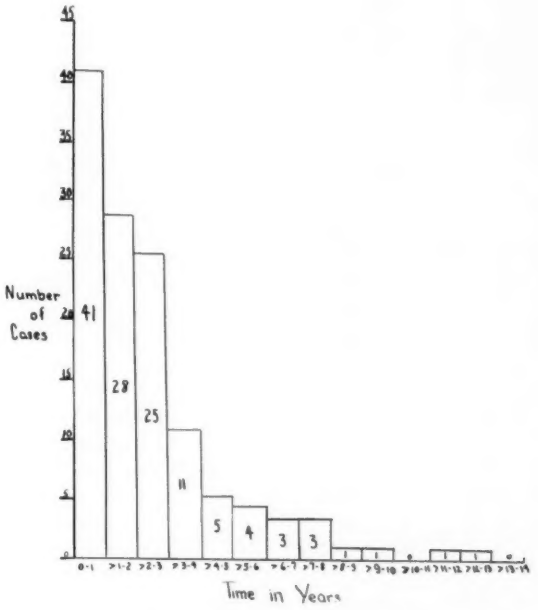


FIG. 3*A*. Interval of time between estimated onset of disease and appearance of recurrences or metastases.

chronological appearance of recurrences or metastases in the course of this disease with a fair degree of uniformity, it is necessary to establish a specific starting point from which the elapsed time will be reckoned. The difficulties encountered in determining the exact time of onset of this disease have been emphasized by Bouchard,[1] who feels that such a determination is practically impossible. In his study, the starting point of the disease was taken as that time at which the patient or physician first felt a palpable mass in the breast which, upon subsequent pathological examination, was found to be cancer. Furthermore, metastases or recurrences were considered to exist only when there was specific roentgenographic evidence of osseous metastases, or when suspicious soft tissue lesions were proved malignant from the breast by biopsy. It is clear that the use of the above criteria for the determination of the time of onset of the disease and the time of appearance of recurrences and metastases will introduce some error in certain cases. It is conceivable, for example, that a palpable mass may be present in the breast for several months or one to two years before the patient becomes aware of it. In fact, in about 2 per cent of patients with carcinoma of the breast, the initial symptoms are due to a metastatic lesion rather than the primary growth.[5] However, in a study of this sort, objective criteria are desirable in order to make the data as reliable as possible. Moreover, the use of the same criteria for all cases tends to make the error uniform within the series.

In Figure 3*A* the interval of time between the estimated onset of disease and the appearance of recurrences or metastases is shown. The average interval for the whole series was two to three years. The data for Figure 3*A* were obtained as follows: Each recurrence or metastasis was tabulated; however, if multiple recurrences or metastases occurred simultaneously or within a relatively short interval (two to three months), this whole group of recurrences

TABLE II

INCIDENCE OF PATIENTS WITH ONE, TWO, THREE OR MORE RECURRENCES OR METASTASES

| | Number of Patients | Per Cent of Total Patients | Per Cent of Patients with Recurrences or Metastases |
|---|---|---|---|
| Total | 100 | — | — |
| Total number of patients with recurrences | 92 | 92% | 100% |
| Number of patients with one recurrence or metastasis | 67 | 67% | 72.8% |
| Number of patients with two recurrences or metastases | 19 | 19% | 20.7% |
| Number of patients with three or more recurrences or metastases | 6 | 6% | 6.5% |

or metastases was tabulated only once. The numerical values in Figure 3*A*, therefore, do not represent the sum total of individual recurrences or metastases, but rather the individual recurrences or metastases or groups of recurrences or metastases occurring at different time intervals. The number of patients represented in Figure 3*A*, *i.e.*, the number of patients in the series who had recurrences or metastases was 92. Table II indicates the number of patients who had one, two or three or more recurrences or metastases. Again, it should be emphasized that this does not refer to one, two or three or more individual recurrences or metastases, but rather to one, two or three or more separated time intervals during which the patient had recurrences or metastases.

Figure 3*A* does not reveal any tendency for a cyclic pattern in the time of appearance of recurrences or metastases. The highest incidence of recurrence and metastasis is within one year of the onset of the disease. Most of these early recurrences and metastases represent disease in axillary and supraclavicular lymph nodes. Figure 4 indicates the most frequent sites of recurrence and metastasis in this series.

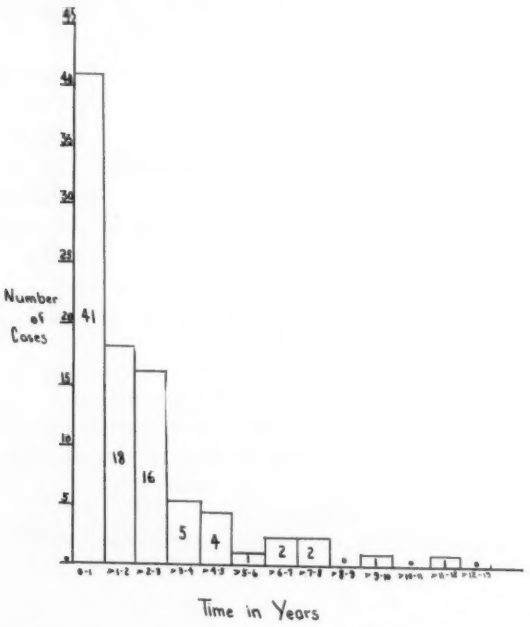


FIG. 3*B*. Interval of time between estimated onset of disease and appearance of first recurrence or metastasis in all patients with recurrences or metastases. (Time of recurrence of one patient not known.)

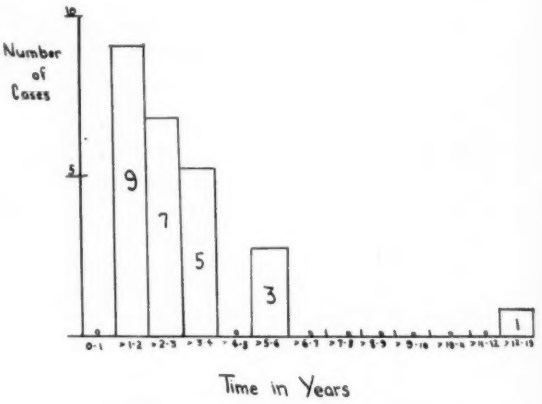


FIG. 3*C*. Interval of time between estimated onset of disease and appearance of second recurrence or metastasis in all patients with two or more recurrences or metastases.

In order to test the possibility that the data in Figure 3*A* might be masking a cyclic tendency in recurrent and metastatic breast cancer, the data forming the basis of Figure 3*A* were broken down to yield Figures 3*B* and 3*C*. In Figure 3*B*, the interval of time between the estimated onset of the disease and the appearance of the *first* recurrence or metastasis in all patients who had recurrences or metastases is plotted. In Figure 3*C*, the same thing is done with respect to the interval of time between the onset of the disease and the *second* recurrence or metastasis in those patients who had two or more recurrences or metastases. In neither of these subsidiary curves is any cyclic tendency revealed. However, the material in Figures 3*B* and 3*C* was subjected to statistical analysis using the nomographs of L. E. Simon, and data in "Engineer's Manual of Statistical Methods" by L. E. Simon. From such a calculation it can be stated that 70 to 90 per cent of those patients who will develop recurrences or metastases from breast cancer will develop the *first* recurrence or metastasis within *three* years after the estimated onset of the disease. Of those patients who will develop two or more recurrences or metastases from car-

TABLE III

RELATIONSHIP BETWEEN TIME OF APPEARANCE OF FIRST AND SECOND RECURRENCES AND METASTASES

| Interval of Time between Estimated Onset of Disease and Appearance of 1st Recurrence | Number of Patients with 1st Recurrences Appearing at Indicated Time | Number of Patients with no 2nd Recurrences | Number of Patients with 2nd Recurrences | Time Interval Between Appearance of 1st and 2nd Recurrences in Those Patients with 2nd Recurrences (in years) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | 0–1 | >1–2 | >2–3 | >3–4 | >4–5 | Arithmetic Mean Number of Years |
| | | | | Number of Patients with 2nd Recurrences at These Intervals | | | | | |
| years | | | | | | | | | |
| 0–1 | 41 | 25 | 16 | 9 | 3 | 3 | 0 | 1 | >1–2 years |
| 1–2 | 18 | 13 | 5 | 4 | 0 | 0 | 1 | 0 | >1–2 years |
| 2–3 | 16 | 14 | 2 | 2 | 0 | 0 | 0 | 0 | 0–1 years |
| 3–4 | 5 | 5 | 0 | — | — | — | — | — | |
| 4–5 | 4 | 3 | 1 | 1 | 0 | 0 | 0 | 0 | 0–1 years |
| 5–6 | 1 | 1 | 0 | — | — | — | — | — | |
| 6–7 | 2 | 2 | 0 | — | — | — | — | — | |
| 7–8 | 2 | 2 | 0 | — | — | — | — | — | |
| 8–9 | 0 | 0 | 0 | — | — | — | — | — | |
| 9–10 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | >2–3 years |
| 10–11 | 0 | 0 | 0 | — | — | — | — | — | |
| 11–12 | 1 | 1 | 0 | — | — | — | — | — | |
| Total | 91* | | | | | | | | |

* Time of appearance of recurrence in one additional patient unknown.

cinoma of the breast, 59 to 96 per cent will develop the *second* recurrence within *four* years after the estimated onset of the disease. The probability for the above limits is 0.99, on the assumption that this is a sample taken at random. Thus, if a patient has survived three years without the development of a first recurrence or metastasis, *she has less than a 30 per cent chance of ever developing a recurrence or metastasis subsequently*. Similarly, if a patient has had a single recurrence or metastasis but has not developed a second within four years after the estimated onset of the disease, *she has less than a 41 per cent chance of ever developing another recurrence or metastasis.*

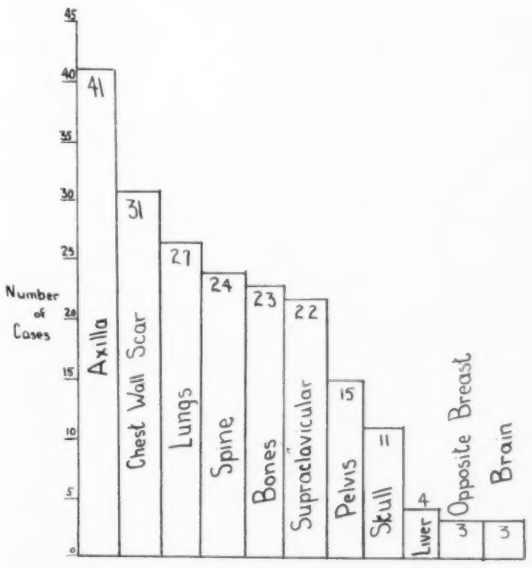


FIG. 4. Sites of recurrences and metastases.

In an attempt to determine whether there was any correlation between the time of appearance of the first recurrence or metastasis and the interval between the appearance of the first and second recurrence or metastasis, the data in Table III were assembled. These data indicate that there is no correlation between the time of appear-

ance of a first recurrence after the onset of disease and the interval between the appearance of the first and second recurrences. Thus, these statistics indicate that an individual whose first recurrence did not appear until late after the onset of the disease has an equal chance of developing a second recurrence very soon after the first or after a prolonged interval after the appearance of the first recurrence.

The above data, therefore, do not indicate any clear cut cyclic tendency for recurrences or metastases when the disease is studied in a group of patients. Such data, however, do not refute the fact that recurrences and metastases may, and in fact do, occur in individual patients in well recognized cycles. The patient who does demonstrate such a cyclic tendency may represent an individual who has developed some type of tissue resistance to a slowly growing tumor and who develops recurrences or metastases when that resistance is lowered for some reason. A similar hypothesis has been suggested by Brown[3] to explain the appearance of late skin recurrences following radical mastectomy for carcinoma. Although a cyclic tendency in recurrences or metastases is often present in a fair number of patients, it is possible, if the time intervals in different patients are spaced properly, that such a tendency would not show up on any curve representing a composite picture from many patients. This possible "masking" of the cycles is represented schematically in Figure 5. Even if such cycles do exist in a considerable number of patients, the time intervals are sufficiently different from patient to patient to offer no prognostic help in an individual case.

Table IV indicates the relation between the type of therapy employed and the average interval of time between the onset of the disease and the appearance of recur-

TABLE IV

ARITHMETIC MEAN NUMBER OF YEARS BETWEEN ONSET OF DISEASE (ESTIMATED) AND APPEARANCE OF RECURRENCES AND/OR METASTASES WITH DIFFERENT TYPES OF THERAPY

| Number of Cases | Type of Therapy | Arithmetic Mean Number of Years between Onset of Disease and Appearance of Recurrence |
|---|---|---|
| 3 | None | 0–1 years |
| 15 | Roentgen therapy alone | >2–3 years |
| 6 | Surgery alone | >1–2 years |
| 76 | Surgery plus roentgen therapy | >2–3 years |

TABLE V

RELATIONSHIP BETWEEN THE AGE OF PATIENT AND ARITHMETIC MEAN NUMBER OF YEARS BETWEEN ONSET OF DISEASE (ESTIMATED) AND APPEARANCE OF RECURRENCES AND/OR METASTASES

| Age of Patients in Years | Arithmetic Mean Number of Years between Onset of Disease and Appearance of Recurrence |
|---|---|
| | years |
| 21–30 | >1–2 |
| 31–40 | >2–3 |
| 41–50 | >2–3 |
| 51–60 | >2–3 |
| 61–70 | >1–2 |
| 71–80 | >2–3 |
| 81–90 | >7–8 |

TABLE VI

RELATIONSHIP BETWEEN AGE OF PATIENTS AND AVERAGE SURVIVAL PERIOD AFTER ONSET OF DISEASE

| Age of Patients | Average Survival Period After Onset of Disease |
|---|---|
| years | years |
| 21–30 | >2–3 |
| 31–40 | >3–4 |
| 41–50 | >3–4 |
| 51–60 | >4–5 |
| 61–70 | >3–4 |
| 71–80 | >4–5 |
| 81–90 | >7–8 |

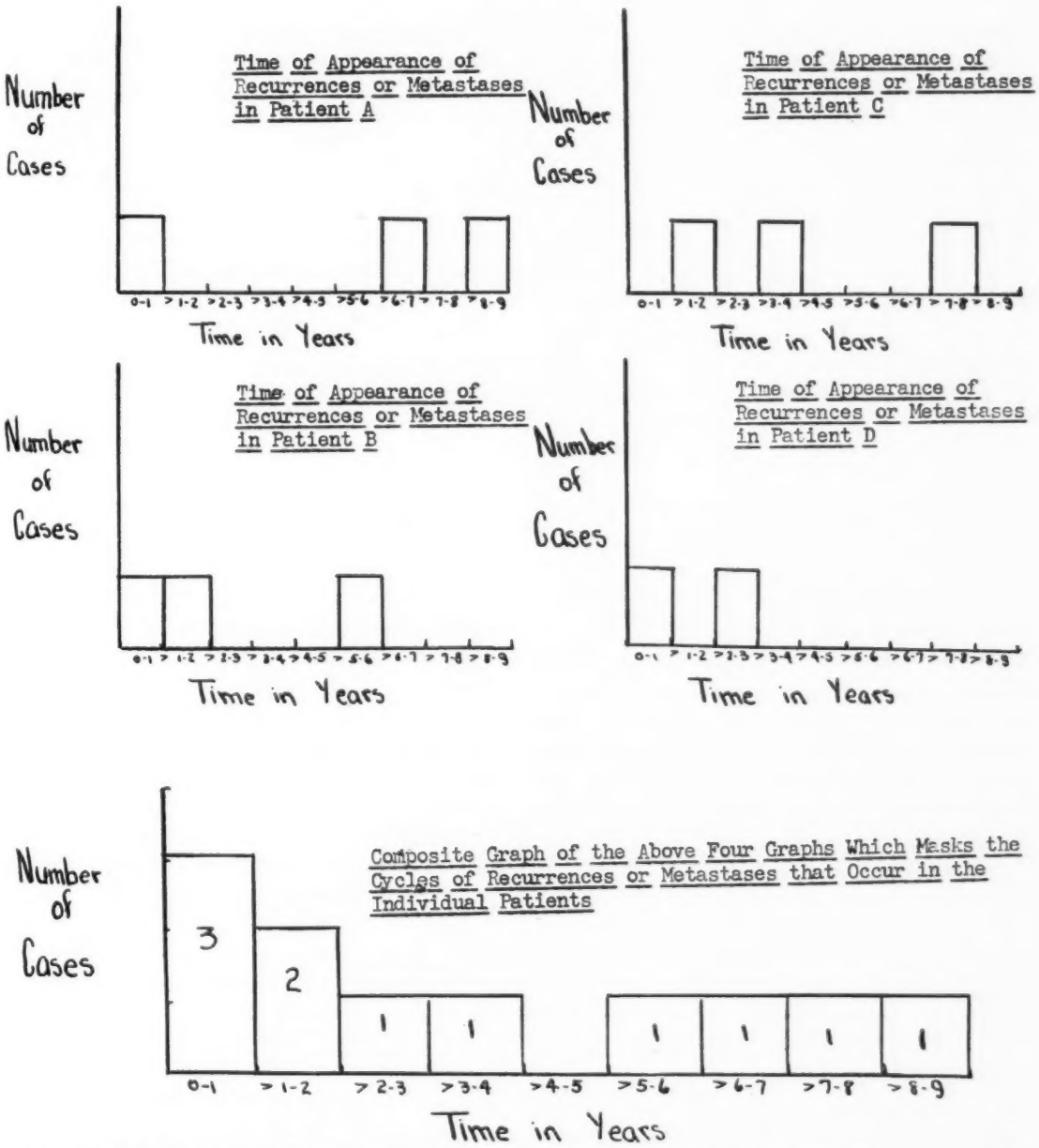
Number of Cases
Time of Appearance of Recurrences or Metastases in Patient A
0-1 > 1-2 > 2-3 > 3-4 > 4-5 > 5-6 > 6-7 > 7-8 > 8-9
Time in Years
Number of Cases
Time of Appearance of Recurrences or Metastases in Patient C
0-1 > 1-2 > 2-3 > 3-4 > 4-5 > 5-6 > 6-7 > 7-8 > 8-9
Time in Years
Number of Cases
Time of Appearance of Recurrences or Metastases in Patient B
0-1 > 1-2 > 2-3 > 3-4 > 4-5 > 5-6 > 6-7 > 7-8 > 8-9
Time in Years
Number of Cases
Time of Appearance of Recurrences or Metastases in Patient D
0-1 > 1-2 > 2-3 > 3-4 > 4-5 > 5-6 > 6-7 > 7-8 > 8-9
Time in Years
Number of Cases
Composite Graph of the Above Four Graphs Which Masks the Cycles of Recurrences or Metastases that Occur in the Individual Patients
3
2
1
1
1
1
1
1
0-1 > 1-2 > 2-3 > 3-4 > 4-5 > 5-6 > 6-7 > 7-8 > 8-9
Time in Years

Fig. 5. Diagram illustrating how a composite graph of 4 patients may mask the cyclic appearance of recurrences or metastases which occurs in the individual patients (theoretical).

rences and metastases. According to these data, those patients who had roentgen therapy alone or surgery plus roentgen therapy had a longer period of freedom from recurrences or metastases than those patients who had no therapy or had surgery alone. This is difficult to understand since of the 6 patients who had surgery alone, 5 were early cases and 4 of these 5 had definitive therapy within a few months after the estimated onset of the disease. On the other hand, many of the cases that had roentgen therapy alone were advanced cases that were considered inoperable. Such data suggest that Chase's concept of "preseeding" of cancer cells in carcinoma of the breast may play an important role in certain cases. According to Chase,[4] dis-

TABLE VII

PER CENT OF EXPECTED SURVIVAL IN YEARS LOST DUE TO CANCER IN VARIOUS AGE GROUPS (FROM U. S. LIFE TABLES FOR WHITE FEMALES, 1939–1941)

| Age at Estimated Onset of Disease | Number of Patients | Average Survival in Years | Expected Survival in Years for Group | Total Survival in Years | Total Loss from Cancer in Years | Average Loss from Cancer in Years | Per Cent of Expected Survival Lost from Cancer |
|---|---|---|---|---|---|---|---|
| years | | | | | | | |
| 21–30 | 7 | 2.5 | 314.3 | 17.5 | 296.8 | 42 | 94.4 |
| 31–40 | 18 | 3.5 | 659.5 | 63 | 596.5 | 33 | 90.4 |
| 41–50 | 33 | 3.5 | 927.8 | 115.5 | 812.3 | 25 | 87.6 |
| 51–60 | 25 | 4.5 | 500.6 | 112.5 | 388.1 | 16 | 77.5 |
| 61–70 | 12 | 3.5 | 150.6 | 42 | 108.6 | 9 | 72.1 |
| 71–80 | 3 | 4.5 | 24.3 | 13.5 | 10.8 | 4 | 44.4 |
| 81–90 | 2 | 7.5 | 9.9 | 15 | −5.1 | −3 | −51.5 |
| Total | 100 | | | | | | |

tant metastases in cancer of the breast have often been seeded before operation, even though there are no palpable lymph nodes on examination and no metastases by the roentgen examination. He points out that such a spread of the disease without clinical involvement is possible since four of the pathways of spread from cancer of the breast do not traverse lymph nodes, *viz:* the mediastinal, transmammary, epigastric and superficial abdominal pathways.

In Tables v and vi, the relationships between the age of the patients, the appearance of metastases and recurrences, and the survival period are pointed out. In a similar analysis for skeletal metastases in cancer of the breast, Bouchard[1] demonstrates that the metastases occurred earlier in the twenty to thirty year age group than in any other age period. Our data do not corroborate this finding, since the shortest interval of time between the onset of dis-

TABLE VIII

PER CENT OF DEATHS ATTRIBUTABLE TO CANCER OF THE BREAST IN THE VARIOUS AGE GROUPS (FROM U. S. LIFE TABLES FOR WHITE FEMALES, 1939–1941)

| Age at Estimated Onset of Disease | Number of Patients Who Died | Number of Deaths Expected within Average Survival Period for Group (from U. S. Life Tables) | Excess Deaths Attributable to Cancer | Per Cent Deaths Attributable to Cancer |
|---|---|---|---|---|
| years | | | | |
| 21–30 | 7 | 0 | 7 | 100 |
| 31–40 | 18 | 0 | 18 | 100 |
| 41–50 | 33 | 1 | 31 | 97 |
| 51–60 | 25 | 2 | 23 | 92 |
| 61–70 | 12 | 1 | 11 | 92 |
| 71–80 | 3 | 1 | 2 | 67 |
| 81–90 | 2 | 2 | 0 | 0 |
| Total | 100 | | | |

ease and the appearance of metastases in our series of patients was present not only in the twenty to thirty year old age group, but also in the sixty-one to seventy age group. Bouchard's data also indicate that the longer the interval between the onset of the disease and the appearance of recurrences or metastases, the longer the survival period. Our data also suggest such a positive correlation, although this is not very striking. It should be pointed out that the data for the eighty-one to ninety year old age group is based on only 2 cases and therefore cannot be considered representative of patients in this age group.

In order to determine how many of our patients' deaths could be directly attributable to cancer, and how many deaths could be accounted for on the basis of the life expectancy of that patient, the data in Tables VII and VIII were compiled. The data in these tables are based on the United States Life Expectancy Tables for White Females for 1939–1941. These tables show very strikingly the large number of "man-years" lost from cancer. In the twenty-one to forty year age period, 100 per cent of the deaths can be attributed to cancer. This, together with the average survival data of Table VI, indicates that cancer of the breast takes a much higher toll and kills in a shorter time among the younger age group than in the older patients. This agrees with the results of investigations by Nathanson and Welch[9] and Lee.[8]

Cancer of the breast metastasizes in several ways. The disease also spreads locally. The methods of local and distant spread may be listed as follows:[2] (*a*) infiltration, whereby the cancer cells infiltrate the interstices between the fat cells and bundles of fibrous tissue; (*b*) lymphatic spread, which may occur in two ways—either by growth along the vessels as described by Handley,[6] or as emboli within the lymph fluid; (*c*) transcelomic implantation whereby cancer cells break out of the lymphatic plexuses of the deep fascia, escape into the serous cavities, and become distributed throughout these cavities by visceral activity, as well as by gravity; (*d*) blood stream emboli, which are especially responsible for osseous metastases. Brown[3] has pointed out that in addition to the above methods of local and distant spread, local skin recurrences in carcinoma of the breast may be due to implantation of tumor cells into the skin at the time of surgery. If this latter mechanism is an important factor, it becomes evident that the time of appearance of local recurrences will, in certain instances, depend upon the surgical technique employed during the removal of the tumor.

## SUMMARY

1. One hundred patients with cancer of the breast, one of whom is living at the present time, are reviewed with special emphasis on the time of appearance of recurrences and metastases after the estimated onset of the disease.

2. The peak age incidence in the group was in the forty-one to fifty year decade.

3. Seventy-six per cent of the patients had surgery plus roentgen therapy; 15 per cent had roentgen therapy alone; 6 per cent had surgery alone; 3 per cent had no therapy.

4. Roentgen therapy added to surgery did not improve the survival rate.

5. The arithmetic mean number of years between the estimated onset of the disease and death for the group as a whole was three to four years.

6. The arithmetic mean number of years between the onset of disease and the appearance of recurrence or metastasis was two to three years.

7. Seventy to 90 per cent of those patients who will develop recurrences or metastases from cancer of the breast will develop the first recurrence within three years after the onset of the disease. Fifty-nine to 96 per cent of those patients who will develop two or more recurrences or metastases from cancer of the breast will develop these within four years after the estimated onset of the disease.

8. No clear cut cyclic tendency in the

appearance of recurrences or metastases is demonstrated.

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We wish to thank Dr. E. Douglass Burdick, Assistant Professor of Vital Statistics and Biometry, School of Medicine, University of Pennsylvania, for his assistance in the statistical analysis used in this report. His help was invaluable.

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Vol. 70, No. 3

# SIGNAL SKELETAL METASTASES FROM RENAL CARCINOMA

## A REPORT OF THREE CASES WITH SPECIAL ROENTGEN FEATURES*

*By* CHARLES W. McCLANAHAN, M.D.,† *and* LOUIS J. BONANN, M.D.‡

THREE most interesting and very similar cases of metastatic neoplasm have recently been observed on the Radiological Service of the General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles. The coincidence of repetition in a comparatively brief period of time was most fortunate, these 3 cases having been observed during a period of nine months. The clinical resemblance between the first and second case was so striking that in the second case the diagnosis was immediately suspected, and on the third occasion the diagnosis was presumed almost before the films were dry.

The presenting symptoms, complaints, and physical findings were nearly identical. In addition, in all cases the site of the signal metastasis lay in the same segment of the same extremity.

A brief résumé of each case with complete roentgenographic findings follows (photographs of available gross specimens and microscopic sections are included in the illustrations for correlation with the roentgen features).

### REPORT OF CASES

CASE 1. J. M., a fifty-four year old white carpenter, entered the hospital on January 6, 1948, complaining of painless swelling of the left arm of about one year's duration. He stated that the roentgen examination of the initial swelling of his arm had revealed a fracture of the lower end of the long bone. The arm had been immobilized in plaster for six months during which time it had become twice as large as normal. The swelling continued progressively and painlessly. On admission it was three times the size of the right arm (Fig. 1). History disclosed no significant subjective symptoms during this period except the observed enlargement.

FIG. 1. Case 1. Physical appearance of the marked fusiform enlargement of the left arm on admission.

Past history disclosed one previous admission to this hospital in 1941 for medical treatment of varicose veins of both legs. Review of the hospital chart revealed no significant findings and the laboratory procedures at that time were all essentially negative. The urinalysis reports were entirely negative. The principal objective finding was listed as a moderately severe, bilateral stasis dermatitis presumably due to the varicosities. Rupture of these varices occurred,

* From the Department of Radiology, Wadsworth General Hospital, Veterans Administration, Los Angeles, California. Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

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FIG. 2. Case 1. Granulomatous fungating growth present on medial aspect of the left leg on admission.

producing small exuberant growths which gradually disappeared. The large growth on the left leg the patient believed to be one of these lesions which had not receded (Fig. 2).

*Physical Examination.* Examination revealed a poorly nourished, sallow-skinned white male who appeared much older than his fifty-four years. The conspicuously enlarged left arm was supported against his side with his right hand. Heart and lungs were essentially negative. The radial and pedal pulses were readily palpable bilaterally. There had been a gradual, general weight loss of from 80 to 100 pounds. A growth on the lower aspect of the left leg was discovered during the physical examination (Fig. 2). This had been there since August, 1947. The abdomen was flat with no scars or visible abnormalities. No tenderness was elicited and no masses were palpable. The genitalia and rectal examination were entirely negative. Inspection of the back revealed slight swelling and tenderness over the right side at the level of the second and fourth lumbar vertebrae. There was no coastal vertebral angle tenderness.

The right arm was of normal size and measured approximately 10 inches in circumference. The lower half of the left arm was diffusely enlarged (Fig. 1) with a measured circumference of 17 inches. The swelling was not tender and no abnormal pulsation was visible. There was marked superficial venous congestion as illustrated by the infrared photograph (Fig. 3). A soft thrill was palpable over the entire extent of the brachial artery with a bruit audible over the axillary and subclavian arteries. No neurological or significant arterial impairment was detected. There was very limited flexion of the fingers, wrists, and especially the elbow.

The skin of the lower extremities was dry and pigmented with brownish discolorations as shown in Figure 4. The photograph indicates the character of the odorous, partially necrotic granulomatous tumor present on the medial aspect of the left leg. A soft subcutaneous swelling about 1 inch in diameter was present just below the angle of the right scapula. It resembled a lipoma or sebaceous cyst. Several large matted and tender lymph nodes filled the left axilla.

*Laboratory Studies.* The blood count showed a moderate anemia with a slightly elevated white count. Routine urine examinations were negative except for an occasional white blood corpuscle. Calcium was present in the routine

FIG. 3. Case 1. Infrared photograph showing the marked generalized venous engorgement over the entire arm and precordium.

urine samples, but no quantitative estimation was made. Total serum proteins were 5.7 gm. with an A/G ratio of 1.3:1. Serum alkaline phosphatase was 3.1 units[28] and serum acid phosphatase was 1.9 units. Serum calcium was 11.1 mg. per cent. Inorganic phosphorus was 3.3 mg. per cent. The cephalin flocculation test was negative.

Roentgen examination of the left arm revealed a large fusiform tumor mass of soft tissue density completely replacing the lower half of the humerus (Fig. 5). Fragments and strands of calcium streaked through the tumor substance. A complete skeletal survey revealed no other osseous involvement, and there was no roentgen evidence of pulmonary metastasis. Only a small area of periosteal thickening was evident over the lower end of the left tibia at the site of the soft tissue tumor (Fig. 6).

The patient was presented at Staff Conference and to the Hospital Tumor Board. It was the consensus that the tumor was probably a primary chondromyxosarcoma of the left humerus. The possibility of a separate malignancy of the left lower leg was considered and a biopsy from the fungating leg lesion was suggested. Biopsies were obtained from both sites and opinion concerning frozen section indicated malignant tumors of the same type of undetermined origin. Thereupon, the left arm was disarticulated at the shoulder (Fig. 7), and the tumor of the leg was locally excised. The disarticulated humerus was sectioned longitudinally (Fig. 8), and the roentgen-ray characteristics are shown in the roentgenogram of the specimen (Fig. 9). The pathologist indicated the correct diagnosis from his microscopic studies. Serial sections revealed a clear-cell type carcinoma from both sites, probably metastatic from the kidney or adrenal. Subsequent excretory and retrograde pyelographic studies demonstrated a tumor of the right kidney (Fig. 10).

Fig. 5. Case 1. Initial roentgenogram of left arm shows complete replacement of the distal shaft of the humerus by soft tissue tumor mass with coarse calcific septa varigating the lesion.

Fig. 4. Case 1. Bilateral stasis dermatitis present on both legs from chronic varicosities with the fungating mass unchanged following limited roentgen therapy.

In view of the absence of any other visible skeletal or pulmonary metastases, the Tumor Board recommended the removal of the kidney, to be followed by amputation of the left leg below the knee. The patient refused to submit to this additional surgery and was dismissed.

He returned some three months following his

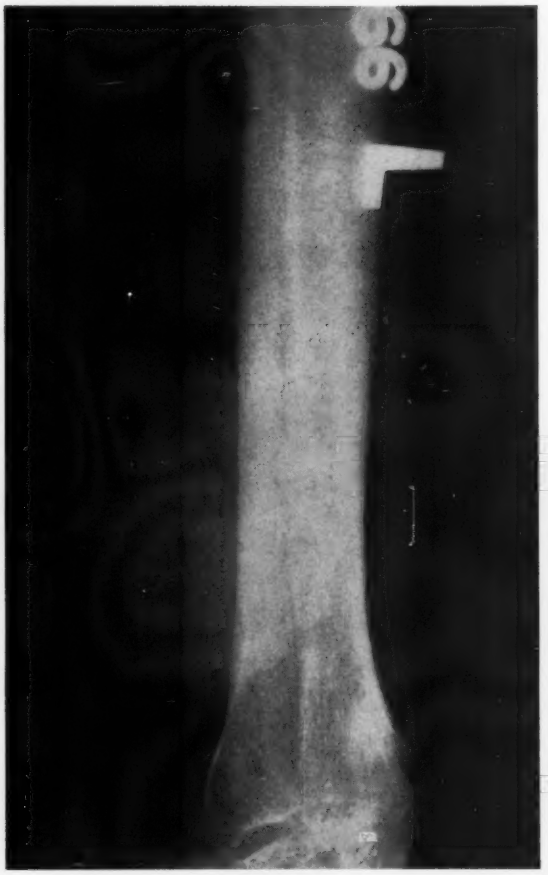

FIG. 6. Case 1. Roentgenogram of the left lower leg shows the gross resemblance of the soft tissue mass on the lower leg to the lesion replacing the shaft of the humerus; slight periosteal thickening is barely perceptible at this site.

FIG. 7. Case 1. The disarticulated left arm with the tumor mass exposed by a skin flap over the site of the fusiform expansion. The radial nerve is stretched taut over the periphery of the lesion.

FIG. 8. Case 1. A longitudinal section through the disarticulated humerus shows the gross appearance of the tumor tissue replacing the bone.

Fig. 9. Case 1. Roentgenogram of the sectioned humerus demonstrates the cartilaginous-like density of the lesion.

discharge complaining that the lesion on the left lower leg had reappeared during the past two weeks and had rapidly become necrotic. A skeletal survey and chest roentgenograms revealed no visible evidence of metastasis. Urinalysis which had previously been normal now showed numerous white and red blood cells and a trace of albumin. He again refused surgery. A course of palliative roentgen therapy was given to the left leg and the right kidney region. There was fairly good resolution of the cutaneous mass. After approximately one month of hospitalization he was discharged.

He again returned approximately three months later. The tumor on the leg had broken through the skin and was bleeding. The chest film at this time revealed a visible metastasis in the left lower lung field. His condition deteriorated rapidly, and he died on February 13, 1949, thirteen months after his initial admission.

*Postmortem Examination.* Examination revealed a large lobulated tumor mass in the lower pole of the right kidney, measuring 11.5 by 9.5 by 7.5 cm. (Fig. 11). Microscopic examination confirmed the diagnosis of hypernephroma (Fig. 12 and 13). A large tumor thrombus was present in the right renal vein which extended to the inferior vena cava. In addition to the known metastases to the left leg and lungs, multiple metastases were found in the liver, adrenals, thyroid gland, and left kidney with regional lymph node extension.

*Final Diagnosis.* Hypernephroma, right kidney, with metastases to the left humerus, left leg, lungs, adrenals, thyroid, liver, and left kidney, with extensive regional lymph node involvement.

Case II. W. B., a fifty-nine year old white dairyman, was admitted to the hospital on

Fig. 10. Case 1. Retrograde pyelogram shows elongation and displacement of the major calyces of the right kidney with distortion of the renal pelvis and clubbing of the minor calyces. Conclusion—Primary parenchymal tumor.

FIG. 11. Case 1. Postmortem specimen of the right kidney divided longitudinally with complete replacement of the lower pole by tumor distinctly demarcated from the renal pelvis.

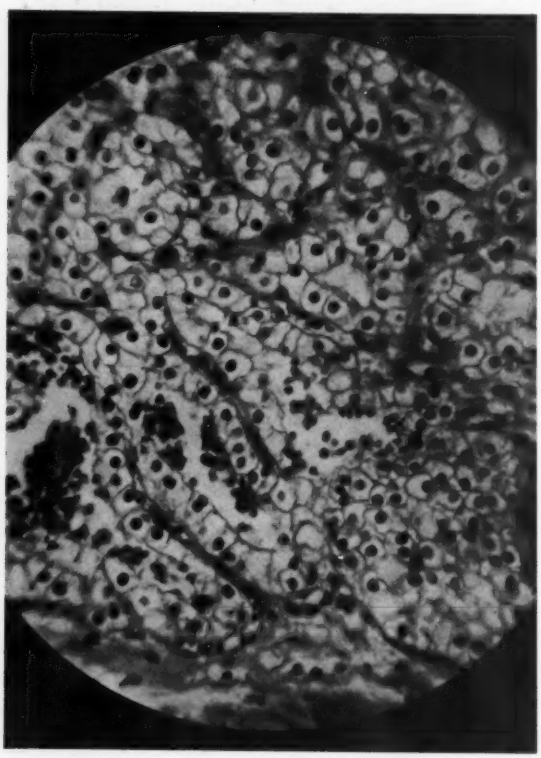

FIG. 12. Case 1. High power photomicrograph of the tumor in the lower end of the humerus shows the predominant clear-cell structure of the metastasis.

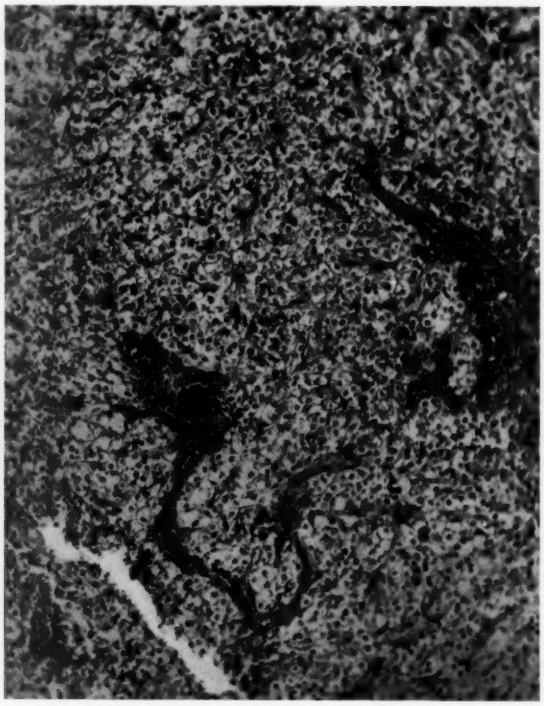

FIG. 13. Case 1. Photomicrograph of the primary tumor replacing the lower pole of the right kidney with predominance of small pleomorphic cells with clear cytoplasm and distinct cell walls and a tendency to tubular arrangement. Conclusion—Hypernephroma.

January 26, 1948, in a semi-stuporous condition caused by an overdose of sedative. He had been perfectly well until August, 1947, when he sustained a fracture to his left arm following insignificant trauma. The fracture had been immobilized in a hanging cast for two months in a hospital in New York. However, there had been no healing during that interval. Surgery was undertaken at that time and bone chips were placed in the fracture site from the left tibia. He was told that biopsy material obtained during that procedure revealed a tumor. Retrograde pyelographic studies disclosed a right renal tumor. Roentgenograms revealed an osteolytic defect in the lower end of the left humerus.

Review of the past history revealed no significant symptoms. The patient had been entirely free of urological complaints except for occasional nocturia. At no time was hematuria noted. There had been a loss in weight of 15 pounds since the occasion of the fracture. Four years previously he had developed a penile sore for which he was not treated until two years later, when a routine dairy plant physical ex-

amination revealed a positive Wassermann reaction.

*Physical Examination.* There was a firm fusiform swelling of the left lower arm with considerable local tenderness, crepitus and ecchymosis (Fig. 14). Moderate tenderness was present over the entire aspect of the right clavicle. A firm round mass about 4 cm. in diameter was palpable over the anterior margin of the right lower rib cage. The abdomen was distended and the liver edge was palpable well beyond the right costal margin. Below this projected a fairly well circumscribed rounded abdominal mass.

*Laboratory Studies.* There was a 1 plus albuminuria with a large number of white blood cells and occasional coarse granular casts in the urine. The blood study showed a normal red cell count and a white cell count of 14,800 with a moderate shift to the left. The Kahn and Wassermann reactions were both positive. Blood chemistry studies included B.U.N. 12 mg. per cent and inorganic phosphorus 3.6 mg. per cent. A/G ratio 1.5:1.

Roentgen study of the left arm revealed a large osteolytic lesion completely replacing the distal third of the left humerus (Fig. 15). A small osteolytic lesion was present in the outer third of the right clavicle surrounded by some callus formation. There was no evidence of pulmonary metastasis.

Fig. 14. Case 11. Appearance of the left arm on admission with visible fusiform swelling just above the elbow.

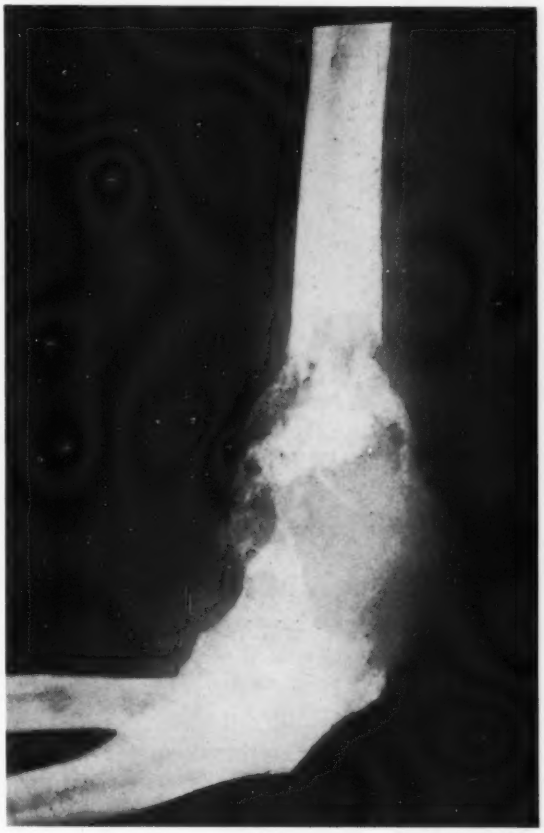

Fig. 15. Case 11. Roentgenogram of the left arm showing a large osteolytic defect with complete obliteration of bone by tumor metastasis in the distal end of the humerus.

Tumor Board evaluation concluded that, considering the widespread metastases, the case warranted only palliative therapy. The patient showed progressive weakening and rapid deterioration.

Death from bronchopneumonia occurred on April 4, 1948, eight months after the pathological fracture of the humerus had taken place.

*Postmortem Examination.* Autopsy disclosed a fairly large, rounded, nodular, encapsulated tumor mass about 12 cm. in diameter in the lower pole of the right kidney (Fig. 16). The mass displaced the entire parenchyma and encroached upon the lower calyces. The gross specimen of the large metastasis in the distal end of the humerus is shown in Figure 17. The mass completely replaced the lower diaphysis with only the articular surface of the trochlea and capitulum spared. Numerous widely disseminated, osseous metastases riddled the skeleton, including the skull and thoracic and lum-

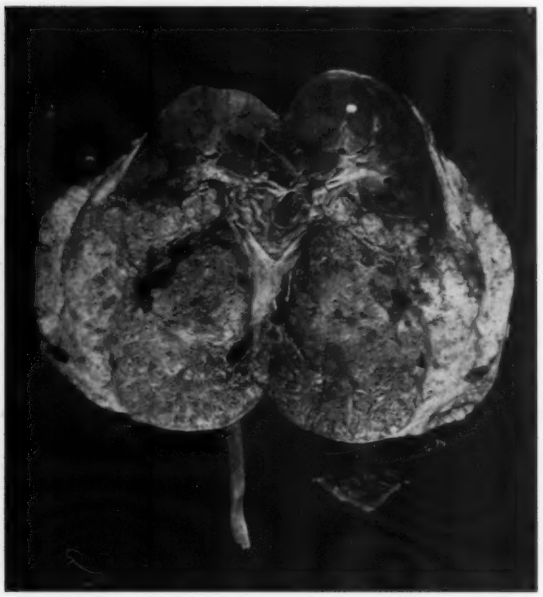

FIG. 16. Case II. The right kidney sectioned to show the rounded encapsulated tumor mass within the lower pole. The right adrenal gland is shown just below the lesion.

bar vertebrae. The distribution of the metastases was not confined to bone but had involved the liver, adrenals, myocardium, and lungs. Miliary lesions were diffusely scattered throughout both lower lobes of the lungs. A few nodules measured 3 cm. in greatest diameter. Microscopic sections of the primary tumor were interpreted as carcinoma, apparently of renal tubercle origin (Fig. 18).

*Final Diagnosis.* Papillary adenocarcinoma, right kidney, with widely disseminated osseous and visceral metastases, and a single large osteolytic metastasis to the left humerus with pathological fracture.

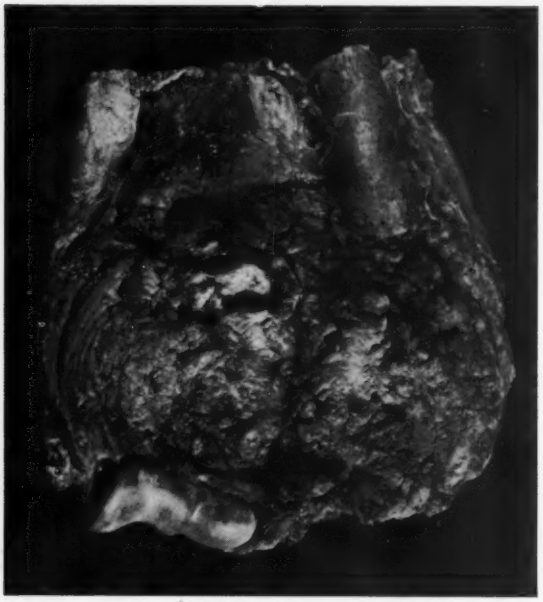

FIG. 17. Case II. The distal end of the left humerus with the metastatic lesion replacing the entire shaft sparing only the articular surfaces of the trochlea and capitulum.

FIG. 18. Case II. Microscopic section taken from the metastatic focus in the left humerus shows the predominant clear-cell tumor formation. Diagnosis—Papillary adenocarcinoma.

CASE III. J. N., a fifty-nine year old Negro janitor, appeared at the Out-Patient Department of the Hospital on September 9, 1948, with the chief complaint of severe pain in the left arm. He had been in excellent health until two weeks previously when he developed a dull aching pain in the left arm. There had been slight swelling at that time but he ignored it, although the size increased during that period. He continued his work as a window washer until the day of his admission. On that morning while getting into his coat, he felt, and distinctly heard, a sharp snap in his left elbow.

*Physical Examination.* A fairly large fusiform

swelling of the lower end of the left arm was visible. The mass was hard and very tender, and crepitation was felt on passive motion. The only other significant physical finding was a questionable abdominal mass just palpable to the left of the midline at the level of the umbilicus.

*Laboratory Studies.* The blood count was normal. Urinalysis was entirely negative. There was no Bence-Jones proteinuria and the Kahn reaction was negative. The blood chemistry studies revealed serum calcium of 11.2 mg. per cent and inorganic phosphorus of 4.1 mg. per cent. Serum acid phosphatase was 10.3 units and serum alkaline phosphatase 1.9 units.

Roentgen studies of the left arm revealed a large fusiform osteolytic defect expanding the shaft of the distal third of the humerus. Coarse trabeculae "honeycombed" the bone simulating a septate pattern (Fig. 19). Some periosteal thickening along the affected cortical portion was visible.

Fig. 19. Case III. Roentgenogram of the left arm shows a large osteolytic lesion expanding the distal shaft of the humerus with coarse trabeculae honeycombing the bone, producing a septate appearance. The fusiform soft tissue swelling is visible surrounding the distal half of the humerus.

Fig. 20 Case III. Excretory pyelogram shows abnormal enlargement of the left kidney silhouette with marked calyceal distortion and separation indicating a primary renal tumor.

A skeletal survey was entirely negative and there was no evidence of pulmonary metastases. In view of the previous two cases a possible metastatic renal lesion was suggested.

Excretory urography disclosed an enlargement of the lower pole of the left kidney with marked compression, separation, and elongation of the renal calyces (Fig. 20).

The Tumor Board recommended nephrectomy and roentgen therapy to the left arm. The removed left kidney measured 13 by 8 by 6 cm. A bulging, fairly well circumscribed mass 7 cm. in diameter occupied the lower pole of the kidney. The tumor completely replaced the parenchyma and stretched and displaced the lower calyces (Fig. 21). No actual invasion of the calyces was found. Microscopic sections revealed a predominantly multinucleated clear cell alveolar formation indicating a primary renal carcinoma (Fig. 22).

High voltage roentgen therapy to the left lower humerus was palliative. There was no significant visible alteration of the fusiform swelling, although the roentgenograms showed

FIG. 21. Case III. Postoperative specimen shows the well encapsulated lesion occupying the lower pole of the left kidney.

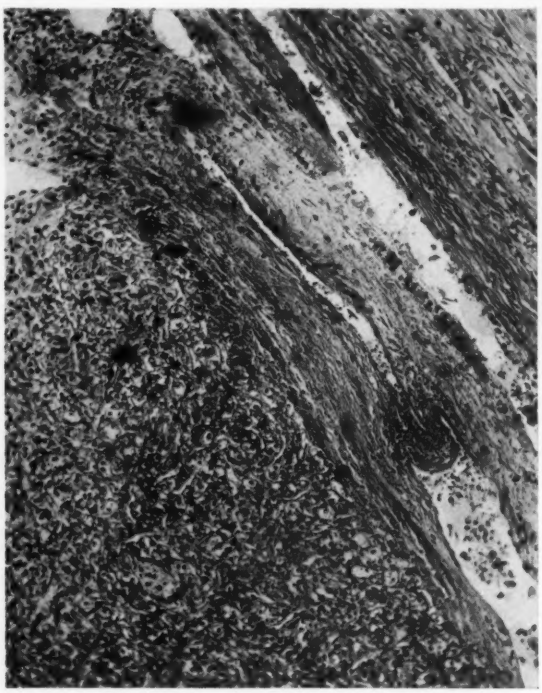

FIG. 22. Case III. Photomicrograph of the lesion occupying the lower pole of the left kidney shows a predominance of multinucleated clear cells with an alveolar arrangement. Diagnosis—Hypernephroma.

some increased sclerosis and barely perceptible filling in of the osteolytic defect.

Following completion of irradiation the Tumor Board reviewed the patient's condition and advised disarticulation of the left arm. This opinion resulted from the combined surgical and pathological consultation which stressed no evidence of local infiltration. Roentgenographically there was no evidence of additional metastases.

The disarticulated left arm (Fig. 23) showed an intramedullary mass of grayish-white tumor tissue which had expanded and "honeycombed" the bone. The cortex was fragmented along

FIG. 23. Case III. Humerus of the disarticulated left arm sectioned longitudinally demonstrates the gross appearance of the intramedullary mass, expansion of the shaft, disruption of the cortical margins, and septation of the medulla.

both borders and appeared paper-thin immediately surrounding the mass.

Recovery was uneventful and the patient was discharged from the hospital. In periodic follow-up examinations by the Tumor Board, he has been asymptomatic with no weight loss. His general health has been good, the only complaint being some persistence of phantom pain. The operation sites are well healed and no abdominal masses are palpable. However, the

chest roentgenogram showed a questionable density in the lower left lobe, but there has been a gradual resolution of this density, which was assumed to have been a segmental pneumonitis. The patient has been observed closely for the past two years. At his last examination in September, 1950, twenty-four months since nephrectomy and twenty-two months following the disarticulation, there was no evidence of metastasis or recurrence, and the chest roentgenogram was completely negative.

## HISTORICAL REVIEW

Contrary to expectations, the solitary skeletal metastasis from renal carcinoma is not a rarity. The literature is studded with original articles and case reports recording this phenomenon as a well established medical observation.

Attention was first focused on such cases by Albrecht[2] in 1905, when he reported a case with a hyperplastic type of metastasis in the occipital bone confirmed at autopsy. Another patient returned to him, four years following nephrectomy for hypernephroma, with a single apple-sized metastasis in the scapula. The scapula was excised and ten years later the patient was well and apparently free from any detectable metastasis.

Scudder[26] followed in 1906 with a report of a case in which a complete shoulder joint disarticulation had been performed for a growth in the upper end of the humerus. The patient died just short of five years later, and only a complete postmortem disclosed a left kidney as large as two adult fists. No metastases were found in any other part of the body. Scudder reported 10 other cases of hypernephroma from the Massachusetts General Hospital with 4 of these showing solitary bone metastases. His review of the literature to that date disclosed only 15 authentic cases of bone metastasis in hypernephroma. Halstead[20] in 1907 reported 1 other case of renal tumor with a metastasis to the femur as the first symptom.

After this initial impetus, the general trend in the literature emphasized the clinical symptomatology and recognition of renal tumors. Comparatively little was recorded about the skeletal deposits of these tumors until the publication of Gibson and Bloodgood[17] in 1923. They reported 5 cases of metastases to bone and collected 33 cases from the literature to that date. This brought the total of authentic cases compiled from the literature to 38. Dresser[11] in 1925 reviewed 46 cases of hypernephroma studied at the Massachusetts General Hospital over a period of seven years and found skeletal metastases in 6 cases. In addition to these, he located cases by Colmers, MacKechnie and Broster[11] all involving metastases to bone.

During the last decade, reports have been made by several authors among whom are Turner and Jaffe,[30] Copeland,[8] Fort,[13] and Gillies.[18] Herger and Sauer,[21] and Abeshouse and Weinberg[1] have also reported interesting cases. A most revealing report was made in 1946 by Fried,[14] who collected 87 cases of renal cancer from the Montefiore Hospital. Thirty-nine of these cases showed skeletal metastases. In 17 cases the involvement was solitary. In 54 per cent pulmonary, pleural or mediastinal metastases were also present. His primary interest was the effect of roentgen therapy on the bone metastases, and he reported that these lesions showed very little, if any, local symptomatic improvement. In a few instances growth had not even been retarded by irradiation.

## DISCUSSION

The radiologist is accustomed to find metastatic lesions in bone, and he is familiar with the relative rarity of such deposits below the elbow and knee joints. However, the combination of a solitary metastasis with an unrecognized primary tumor presents one of his most challenging diagnostic problems. Published reports emphasize that the metastatic bone lesion from renal carcinoma is nearly always a destructive one with no evidence of osteoblastic reaction. In most cases the roentgen appearance simulates a primary bone tumor. The solitary deposit often exhibits those features attributed to a primary lesion including expansion, invasion, alteration of trabeculation, and periosteal reaction. The clinical possibilities include a formidable list of malignancies. The most frequently encountered diagnostic problem is the exclusion of primary osteogenic sarcoma. No doubt the main difficulty in diagnosis stems from the potentiality of bone to react in many different ways with a great variation in structure.

As regards the method of metastasis to bone, it is probably now accepted that a good majority of cases extend by blood stream rather than by lymph channels. Renal carcinoma has a notorious tendency to grow into the veins, cases having been recorded where the tumor growth has extended along the renal vein to the inferior vena cava and even up to the right heart. The liver is a common site for metastatic extension and it is supposed that dissemina-

tion occurs by retrograde embolism along the portal vein from the inferior vena cava. It would seem that if this were the case in the majority of vascular disseminations, the tumor might deposit itself in the long bones at the sites of the nutrient foramens. This is not always so, as shown by numerous cases with metastases located near the extremities of the bones. This can be accounted for by the fact that malignant cells in the blood stream tend to fall out and settle within the osseous tissue where the caliber of the vessel is smallest. Also, at this site the flow is most greatly retarded and the conditions are more suitable to implantation. The brief for lymphatic dissemination has been shown by several cases and undoubtedly occurs. However, the distribution of secondary growth to distant sites is more logically explained by dissemination via the blood stream.

The bones usually affected, in order of their frequency, are: humerus, spine, femur, pelvis, ribs, bones of feet, skull, and sternum. Single deposits were found usually in the long bones. The nature of the single metastasis is such that it has been initially suspected in less than 40 per cent of the cases compiled from the literature. It was the consensus that there were no typical roentgen changes that characterized renal metastases in bone. In no instance was the diagnosis of renal cancer metastasis made on the basis of the roentgenographic appearance alone. The first case presented here ran the entire gamut of the usual clinical considerations and differential possibilities. The second and third cases were considered immediately only because the similarity of presentation was so striking that its consideration was more than obvious.

Most recently, however, Sherman and Pearson,[27] in a comprehensive study of the material available at Memorial Hospital, have promulgated the idea that renal cancer metastatic to bone might occasionally present certain unique characteristics in the roentgenogram. Their excellent article reviews most of the clinical aspects and fundamental observations known to date. The various roentgenographic features of renal metastases in bone are considered separately and in detail. Any further discussion of these points would be superfluous with this excellent report available for study. However, in view of some of the roentgen findings observed in our cases, it is of interest to consider comparable features related to their observations.

Their series consisted of 36 proved cases of renal cancer metastatic to bone with adequate roentgenographic coverage. A single osseous metastasis was found in 21 cases of this series. In the remaining 15 cases two or more skeletal lesions were found. In 4 patients the metastases were located in the humerus.

The various skeletal deposits are grouped into three distinctly different osseous patterns recognizable roentgenographically.

The *first* and largest group consisted of 18 cases which showed no internal pattern and was conspicuous by the complete loss of osseous tissue at the site of the lesion. These were classified as the *lytic type* of skeletal metastasis.

The *second* group concerned a *patchy type* of osseous lesion which was found in 3 cases. In these cases the pattern showed fine cystic areas of destruction surrounded by nearly normal or "fuzzy" bone.

The *third* group contained 6 cases with lesions in which a *septate type* pattern prevailed. This was characterized by coarse, well formed septa honeycombing the site of involvement.

A study of the roentgenograms of the skeletal metastases in the cases reported here shows that they fit at least two of the three categories of the classification just outlined. The first case, J. M., shows the characteristics of the *septate type* of lesion with a massive soft tissue tumor replacing all of the normal bone, with a few strands and fragments of calcium density variegating the mass. The second case, W. B., represents the *lytic type* of metastasis with complete liquefaction of bone. The third

case, J. N., exemplifies the *septate type* again with an osseous pattern of coarse septa honeycombing the distal third of the humerus. Thus, the two largest groups of the classification are represented in a limited series of 3 cases. It will be most interesting to correlate future reported roentgen findings in similar cases with regard to this classification. It is our impression that Sherman and Pearson will be justified in initiating this possibility for further consideration.

The metastases of renal malignancies, however, are by no means limited to bone. There is apparently no tissue or site within the body which is not susceptible to secondary deposits. Reports are available disclosing metastases to the thyroid gland,[6] to the iris of the eye, and even to the ciliary body.[7] However, the consensus is that the commonest locations of metastases are osseous.

Of special interest is the course to pursue with regard to treatment when a primary kidney tumor is found with a secondary growth already established. If the sole consideration is that these cases almost always terminate fatally after surgery, even before metastatic tumors are present, there would be considerable cause for hesitation. However, it has been shown that occasionally a single bone metastasis has been found at autopsy. This would justify removal of the primary growth and the metastasis when a single secondary bone tumor only is present. Certainly, our third case justifies the possibility of giving the patient this opportunity for prolongation of life.

SUMMARY

Three strikingly similar cases of renal neoplasm metastatic to bone are presented with special emphasis given to the roentgraphic features.

The frequency with which carcinoma of the kidney metastasizes to bone is well recognized and has been reported frequently in the literature. When the cardinal symptoms of renal tumor are wanting, the true nature of the secondary growth may be overlooked, especially if the patient has been asymptomatic. Carcinoma of the kidney is prone to give rise to osseous metastases, which are at times the first evidence of the presence of a tumor. Metastases usually occur via the blood vessels, the tumor cells reaching the general circulation by way of the renal vein. The true significance lies in the frequency with which the secondary bone lesion resembles a primary tumor and gives rise to the first symptom.

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Vol. 70, No. 3

# ON THE ACCESSORY OSSICLES OF THE SUPRAOCCIPITAL BONE

## SOME NEWLY RECOGNIZED ROENTGEN FEATURES OF THE NORMAL INFANTILE SKULL*

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DURING the roentgen examination of 3,800 newborn infants,† shadows of single and multiple small independent bones were found in the occipital cartilage above the foramen magnum in 15 cases. These bones have not been recognized hitherto roentgenographically and have been described anatomically in a single neonatal skull. The nature of these accessory ossicles and their course during the first year of life constitute this report.

The 15 cases have been divided into groups, according to the number of ossicles present during the neonatal period, when the infants were first examined roentgenographically. Group I is made up of 7 cases in which a single ossicle was found; Group II contains 5 cases with two ossicles each; Group III, one case with three ossicles; and Group IV, 3 cases with four ossicles each.

### CASE REPORTS

*Group I. Seven examples of a single accessory ossicle.*

CASE 1. L. W. On the twelfth day of life, a single oval ossicle was demonstrated in the left side of the innominate synchondrosis, just off the mid-sagittal plane (Fig. 1, *A* and *B*). In the edge of the supraoccipital, opposite the upper pole of the ossicle, there was a shallow concavity. The ossicle was nearer to the supraoccipital than to the left exoccipital, 1 mm. compared with 5 mm. The little bone measured 4 by 6 mm. in its greatest cephalocaudal and transverse diameters. As seen in lateral projection, the ossicle projected slightly beyond the outer surface of the supraoccipital and did not project internally beyond the inner surface of this bone.

At sixty-eight days (Fig. 1*C*), the ossicle had increased in size (10 by 12 mm.), and the concavity opposite it in the supraoccipital had deepened. Next to the medial aspect of its upper pole, a tiny bone was now visible in the cartilage, and three small bony foci had appeared laterally well out in the right side of the innominate synchondrosis.

On the 122nd day (Fig. 1*D*), union had begun between the upper pole of the larger original ossicle and the lower edge of the supraoccipital. The smaller and later-appearing ossicles were all poorly defined owing to their partial blending with the lower edge of the supraoccipital.

CASE 2. B. S. On the second day of life, in lateral projection, a scale-like ossicle was disclosed which extended well beyond the outer surface of the supraoccipital (Fig. 2). Its external position and convexity suggested that it was an extension of the outer table of this latter bone over a buckled innominate synchondrosis, and might have originated directly from overlying periosteum or perichondrium. Its small size suggested that it had developed during the last weeks of gestation. At three months this externally placed ossicle was longer and thicker than before.

CASE 3. R. F. In lateral and Towne projections made forty-eight hours after birth, a discrete circular ossicle (Fig. 3), approximately 8 mm. in diameter, was found on the right side of the innominate synchondrosis, near the mid-sagittal plane. It protruded externally beyond the outer surface of the supraoccipital and it did not protrude internally. At twelve months, the ossicle was invisible; apparently it had fused completely with the supraoccipital.

† These roentgen examinations were part of a larger study by Dr. Katharine Merritt on the "Relation of Maternal Infection During Pregnancy to Fetal Malformations" which was supported by the Life Insurance Medical Research Fund, the Rockefeller Foundation, and the Department of Health, State of New York.

These data were presented as part of the David Murray Cowie Memorial Lecture at the University of Michigan, Ann Arbor, Michigan, October 12, 1951.

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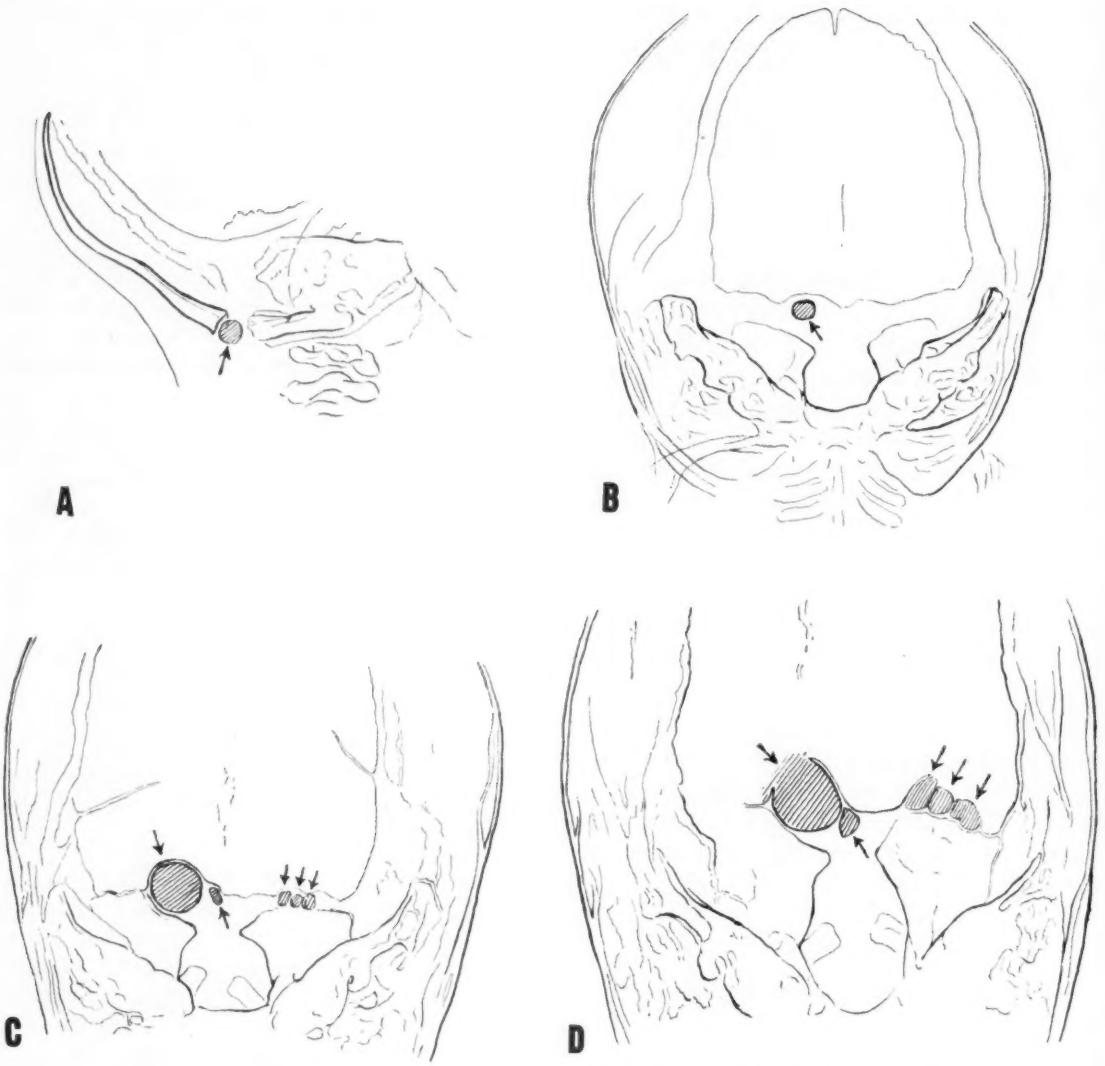



FIG. 1. Case 1. (Tracings of roentgenograms.) Left-sided single ossicle. In (*A*) and (*B*), on the 12th day of life, there is an oval ossicle, and opposite its upper pole, there is a concavity in the edge of the supraoccipital. In (*C*), on the 68th day, the ossicle is much larger and the opposing indentation in the supraoccipital is much deeper. A Kerkring-like ossicle is now visible near the mid-sagittal plane and there are three tiny new ossicles far laterad in the right side of the innominate synchondrosis. In (*D*), on the 122nd day, all of the ossicles have increased in size and they are beginning to fuse with the lower edge of the supraoccipital. Kerkring's ossicle, near the midline, is still independent of the supraoccipital.

CASE 4. P. E. On the twelfth day, a large, single, sharply edged, right-sided ossicle was found near the mid-sagittal plane. It measured 14 by 11 mm. in its greatest cephalocaudal and transverse diameters. Opposite the upper pole of the ossicle, on the edge of the supraoccipital, there was a shallow indentation. As viewed in lateral projection, the ossicle interrupted the normal curve of the occipital arch and projected well beyond the external surface of the supraoccipital in a fashion which might have suggested a fracture fragment (Fig. 4) to one unfamiliar with these little bones in this site.

CASE 5. B. B. S. In lateral and Towne projections, made on the third day of life, a solitary, sharply defined, circular ossicle (9 by 8 mm.) was disclosed on the right side of the

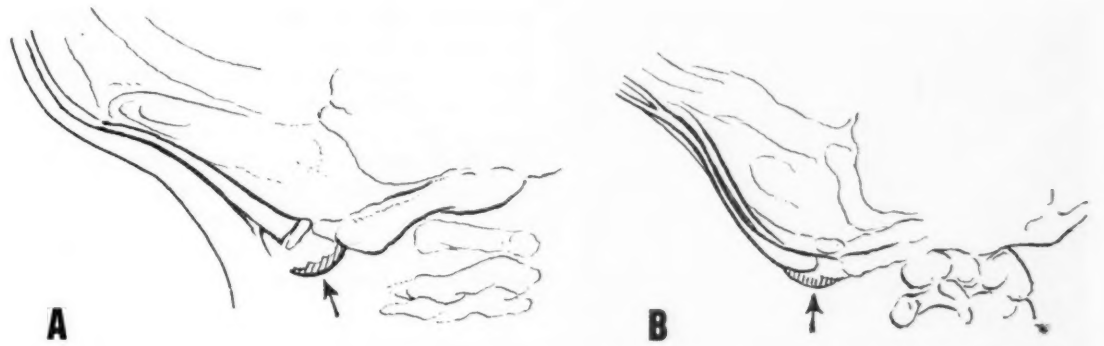



Fig. 2. Case 2. (Tracings of roentgenograms.) Flat scale-like ossicle externally placed in the innominate synchondrosis. (*A*) On the 2nd day of life; (*B*) on the 90th day.

innominate synchondrosis near its mid-sagittal plane. The ossicle projected externally beyond the external surfaces of the neighboring supraoccipital and exoccipital bones.

Case 6. H. C., and Case 7. C. S. Single circular ossicles were demonstrated on the third and fourth days of life respectively. Each measured approximately 5 mm. in diameter. In follow-up examinations during the twelfth month (Case 6) and twenty-sixth month (Case 7), the ossicle in each was invisible, although the innominate synchondrosis in each case was still visible and was represented by a transverse, linear, radiolucent shadow.

*Group II. Four examples of double ossicles.*

Case 8. D. S. On the second and twentieth days of life shadows of two small paired bones were demonstrated in the innominate synchondrosis (Fig. 5, *A* and *B*). Each was located just off the mid-sagittal plane. They were nearly round and measured 10 by 8 mm. and 7 by 7 mm. in their greatest diameters. Between the dorsal poles of the ossicles, a short bony process with a wide base and a pointed free end projected ventrad from the edge of the supraoccipital. This edge was deformed by two shallow indentations, one of which was opposite each of the ossicles. In contrast, there were no

Fig. 3. Case 3. (Tracings of roentgenograms.) Large, right-sided, externally projecting ossicle and small Kerkring's process 48 hours after birth. (*A*) lateral projection; (*B*) Towne projection.

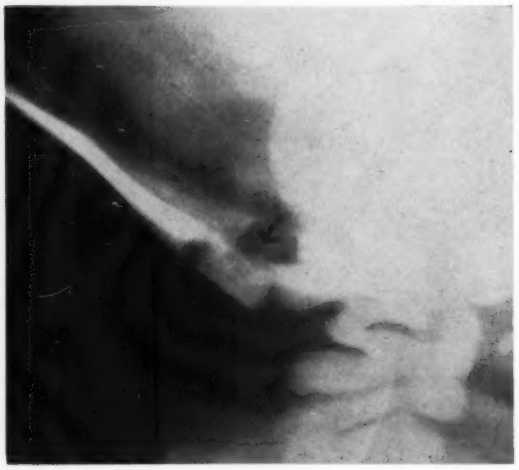


Fig .4. Lateral roentgenogram on the 12th day of life which shows a large externally projecting ossicle which resembles a fracture fragment. In the Towne projection, which is not shown here, this proved to be a smooth, oval ossicle similar to those in Figures 1 and 3.

indentations in the neighboring exoccipital bones, opposite the ventral ends of the ossicles. As viewed in lateral projection, the ossicles protruded externally beyond the external surface of the supraoccipital bone. At six months, the ossicles had grown substantially and measured 20 by 20 mm. in their greatest diameters. They were still separated completely from the edge of the supraoccipital and from each other by fine linear strips of radiolucent cartilage. The bony process in the mid-sagittal plane was difficult to see because it was partially fused with the left ossicle. There was no external bony thickening at the site of the ossicles.

Case 9. M. T. The findings were similar to those in Case 8. The ossicles were, however, situated slightly farther off the mid-sagittal plane. The right ossicle measured 10 by 9 mm. and the left 8 by 7 mm. in their greatest cephalocaudal and transverse diameters.

Case 10. M. R. This infant was born prematurely. The head was not examined roentgenographically until three months after birth, when two pinhead-sized ossicles were demonstrated, each of which was situated far out in the lateral segment of the innominate synchondrosis (Fig. 6). The ossicles were longest in their transverse diameters, which measured about 5 mm.

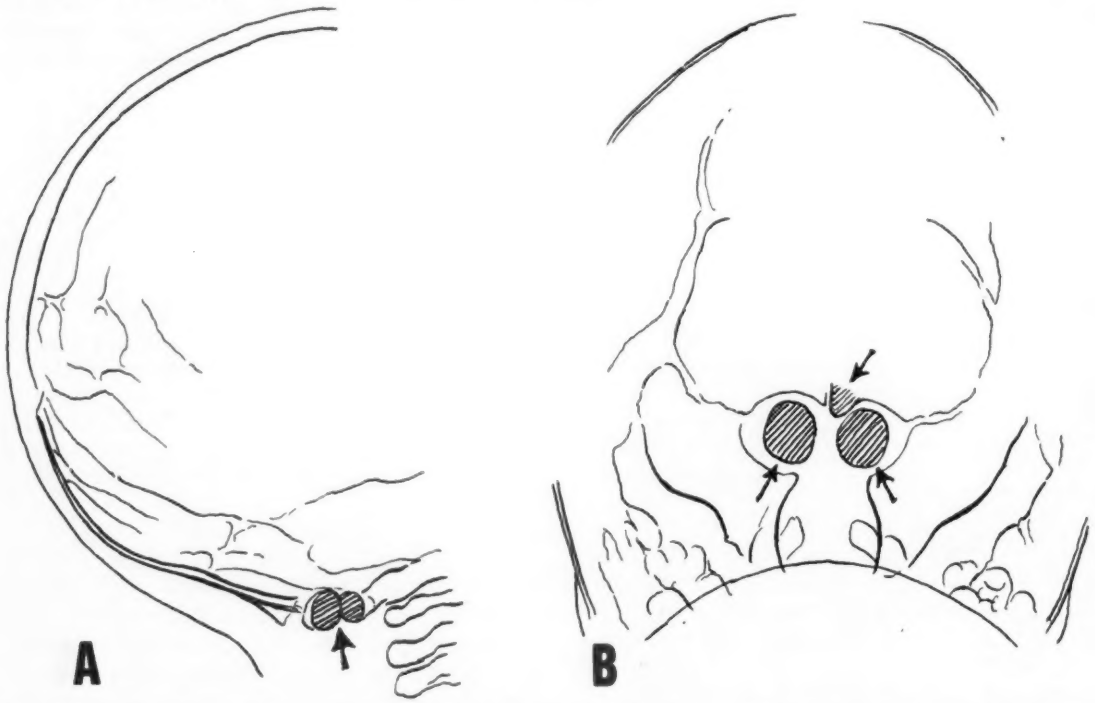



Fig. 5. Case 8. (Tracings of roentgenograms.) (*A*) Lateral projection on the 2nd day of life and (*B*) Towne projection on the 20th day. Large paired medially placed ossicles are visible. In (*B*) a short, pointed Kerkring-like process extends caudad from the lower edge of the supraoccipital.

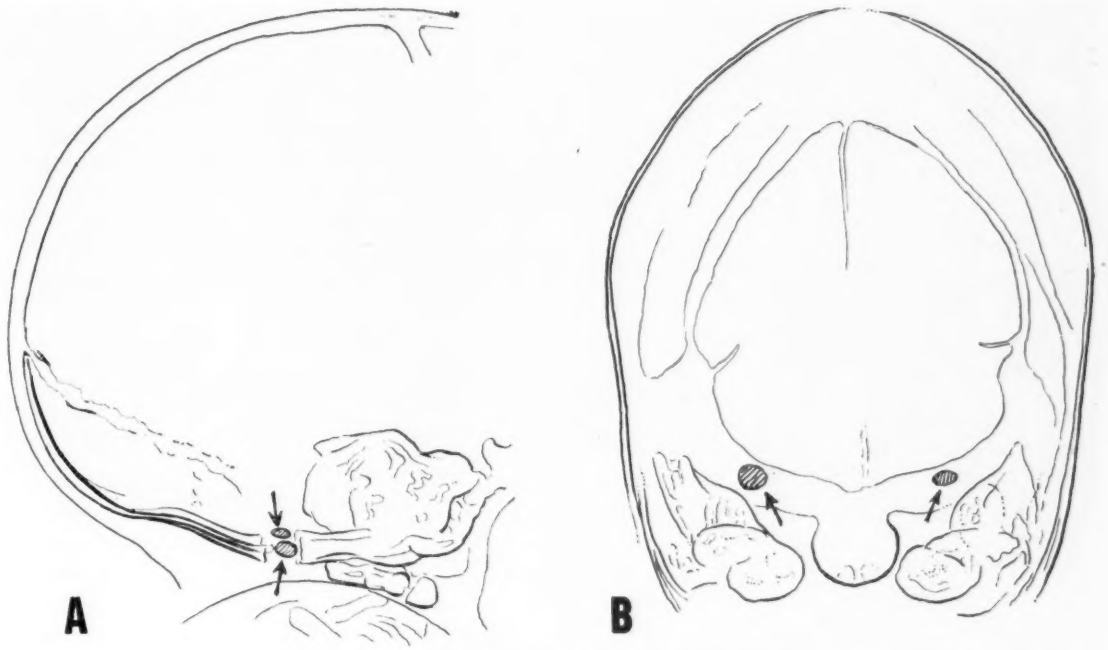



Fig. 6. Case 10. (Tracing of roentgenograms.) In lateral (*A*) and Towne (*B*) projections of the head of a premature infant three months after birth. Tiny, symmetrical and widely spaced ossicles are visible.

Case 11. M. C. Two widely spaced ossicles, similar to those in Case 10, were found on the fifteenth day of life.

*Group III. One example of triple ossicles.*

Case 12. B. S. P. On the seventeenth day (Fig. 7, *A* and *B*), three ossicles were present in the innominate synchondrosis. Two symmetrically placed larger ossicles, each just off the mid-sagittal plane, were similar in size and shape and measured 14 by 9 mm. in their greatest cephalocaudal and transverse diameters. Far out laterally on the right side, there was a third smaller ossicle which measured 7 by 3 mm. Opposite the larger ossicles in the edge of the supraoccipital there were two symmetrical indentations. Between these indentations and also between the medial faces of the larger ossicles, a small bony spine projected caudad from the edge of the supraoccipital in almost the exact mid-sagittal plane, which resembled Kerkring's process. As viewed in lateral projection, the ossicles protruded both externally and internally well beyond the surfaces of the neighboring supraoccipital bone.

At three months (Fig. 7, *C* and *D*), all of the ossicles had increased in size at the expense of the cartilage, and the indentations in the edge of the supraoccipital had deepened. The smaller right-sided, laterally placed ossicle had already begun to unite, by its upper pole, with the opposing edge of the supraoccipital; the larger medial ossicles, in contrast, were still independent of the supraoccipital and of each other. The median bony process, visible on the seventeenth day, had disappeared, but a new, tiny, dense ossicle had appeared between the lower poles of the larger ossicles. Each of the latter measured 22 by 12 mm. The most conspicuous feature at three months was the thick bony swelling which protruded externally and measured 10 mm. at its crest. This thickening of the bony edge of the foramen magnum is not unlike some of the deformities, in the same location in adult skulls, which have been called "occipital vertebras" or partially fused "proatlases."

At six months (Fig. 7*E*), the three ossicles were all larger than before and were buried much deeper into the edge of the supraoccipital. The smaller laterally placed ossicle, which was oval in shape in earlier films, was now triangular. The larger medially placed ossicles were now elongated in their cephalocaudal axes and, transversely, were considerably narrower above than below. They measured 34 by 11 mm. in their greatest cephalocaudal and transverse diameters and had begun to unite with each other at their superior medial faces, and the

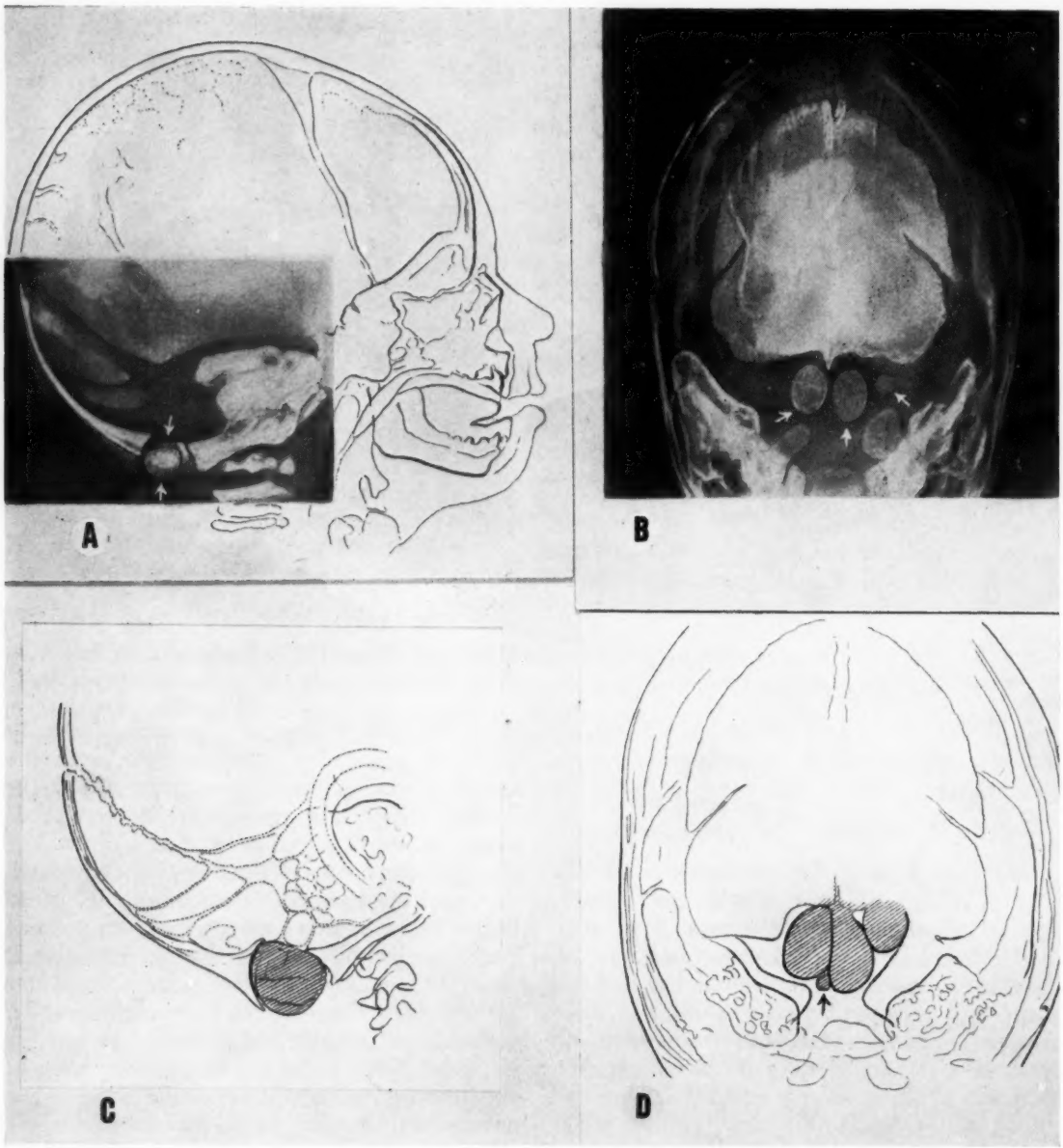
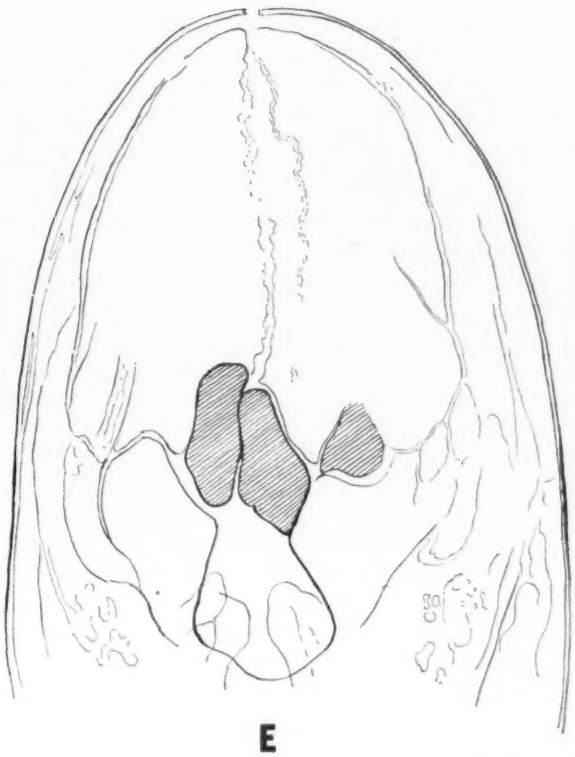


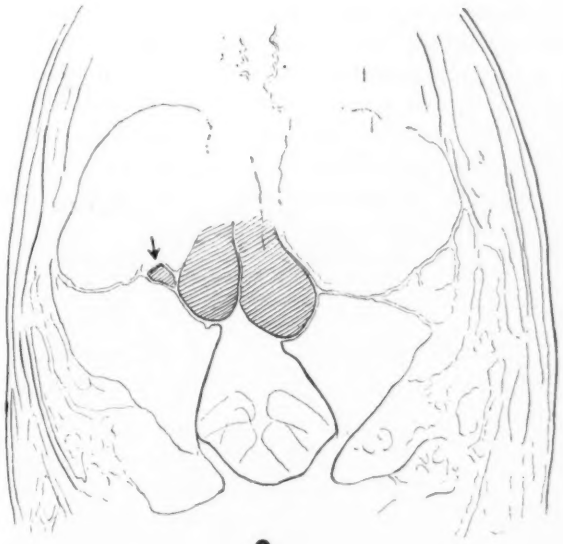

Fig. 7. Case 12. (*A*) and (*B*) are combined tracings and wash drawings of roentgenograms of the head made in lateral and Towne projections on the 2nd and 20th days of life, respectively. There are three ossicles in the innominate synchondrosis, and a small Kerkring-like process near the mid-sagittal plane on the lower edge of the supraoccipital. The edge of the supraoccipital is thickened and cupped (*A*). In tracings (*C*) and (*D*) at 3 months, the ossicles have all grown in size and the edge of the supraoccipital is thicker and more deeply cupped. The large ossicles protrude externally and internally beyond the surfaces of the supraoccipital and exoccipitals. The original Kerkring-like process has disappeared but a new ossicle has appeared near the mid-sagittal plane between the lower poles of the ossicles on the edge of the foramen magnum. All three larger ossicles are beginning to fuse with the lower deeply indented edge of the supraoccipital.

In (*E*), a tracing made at 6 months, the medially placed ossicles have enlarged and elongated cephalocaudally; the laterally placed ossicle has changed from oval to triangular shape; the second Kerkring's os-



E

F



G

sicle has disappeared. Fusion of the ossicles with the supraoccipital is more complete than in earlier observations.

In tracings (*F*) and (*G*), made at 10 months, fusion of the ossicles with the supraoccipital is more complete; the triangular ossicle, seen in (*E*), has disappeared. A new laterally placed smaller ossicle is now visible in the other (left) side of the innominate synchondrosis. External protrusion of the partially fused ossicles and thickening of the edges of the supraoccipital and the exoccipitals are not as pronounced as in (*C*).

tip of the upper pole of the left ossicle was fused to the edge of the supraoccipital. Relatively wide strips of cartilage still separated the ossicles from the upper edges of the exoccipitals. The rounded bony external swelling was still pronounced and had not changed significantly since the third month.

At ten months (Fig. 7, *F* and *G*), the laterally placed smaller ossicle had disappeared by fusion with the supraoccipital. The two medially placed ossicles were partially fused to each other at their upper poles and also to the supraoccipital. Their lower poles were still separated by a radiolucent notch of cartilage. Lateral to the left ossicle a new bone was now visible which measured 7 by 4 mm. The external bony swelling was still clearly visible; it measured 34 mm. in ventrodorsal length and 9 mm. in depth, as viewed in lateral projection.

*Group IV. Three examples of quadruple ossicles.*

CASE 13. R. S. In a lateral projection, made on the third day of life, multiple ossicles superimposed on one another were demonstrated (Fig. 8*A*). The largest measured approximately 10 mm. in its ventrodorsal diameter. The neighboring edge of the supraoccipital was thickened. On the seventeenth day of life (Fig. 8*B*), four large symmetrical ossicles were disclosed in a Towne projection. They were all roughly oval in shape and were longer in their cephalocaudal axes (18 to 13 mm.) than they were in their transverse axes (10 to 8 mm.). Between the two medially placed ossicles in the mid-sagittal plane of the head, a long bony process extended caudad off the edge of the supraoccipital. This process was widest at its base and pointed at its free end. In the pair of ossicles on each side of the midline, the opposing face of each ossicle was flattened, which gave a biscuit-shaped appearance to each pair. The upper pole of each ossicle extended into an indentation in the opposite edge of the supraoccipital. The edges of the exoccipital bones opposite to the lower poles of the ossicles were, in contrast, not indented. In a follow-up examination during the twelfth month, the innominate synchondrosis could still be made out as a transverse radiolucent linear shadow, but all of the ossicles had disappeared. Apparently they had fused completely with one another and with the supraoccipital.

CASE 14. E. C. On the second and seventeenth days of life, four ossicles were demonstrated (Fig. 9). The bones differed from those in Case 13 in that the laterally placed ossicles were considerably smaller (8 by 5 mm.) than

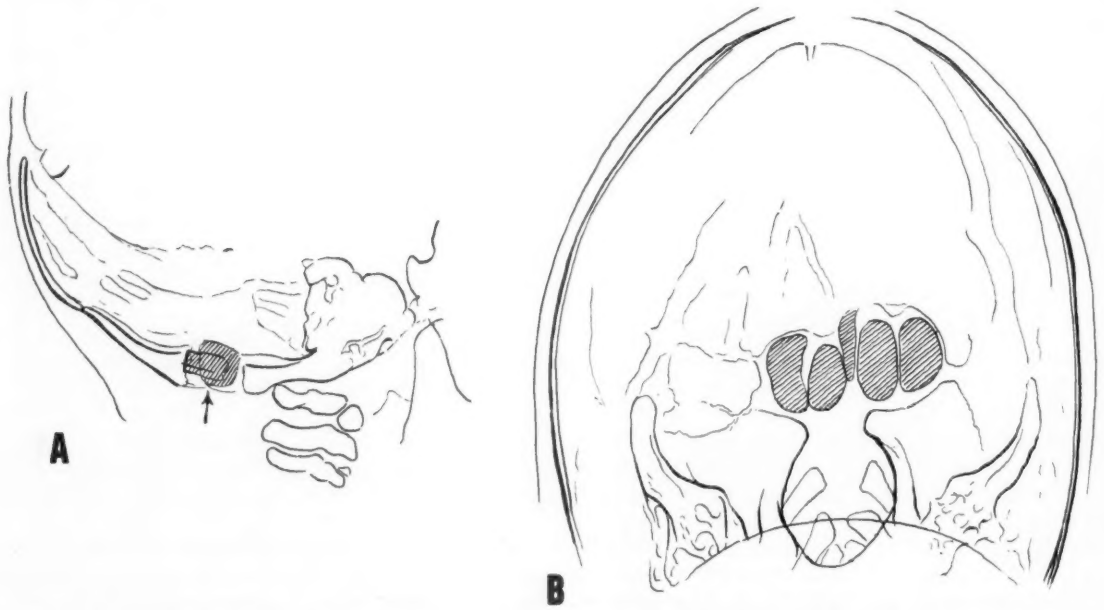



FIG. 8. Case 13. Tracings of roentgenograms in lateral (*A*) and Towne projections (*B*) on the 3rd and 17th days of life respectively. Two pairs of elongated oval ossicles and a large Kerkring-like process are visible in the innominate synchondrosis. The opposing lower edge of the supraoccipital is deeply cupped.

their medially placed counterparts (16 by 12 mm.). At the mid-sagittal plane, a bony process extended caudad off the edge of the supraoccipital and separated the two medial ossicles. Follow-up examinations at six and twelve months disclosed gradual disappearance of the cartilage in the innominate synchondrosis and fusion of the ossicles with the supraoccipital and with one another. These fusions were complete at one year.

Case 15. L. M. The findings were similar to those in Case 14. Of the four ossicles, the medially placed pair on each side of the mid-sagittal plane were larger. In this patient, however, the two medially placed ossicles were different in size. The right ossicle was larger and measured 15 by 12 mm., in contrast to the smaller diameters of 10 by 7 mm. of the left ossicle.

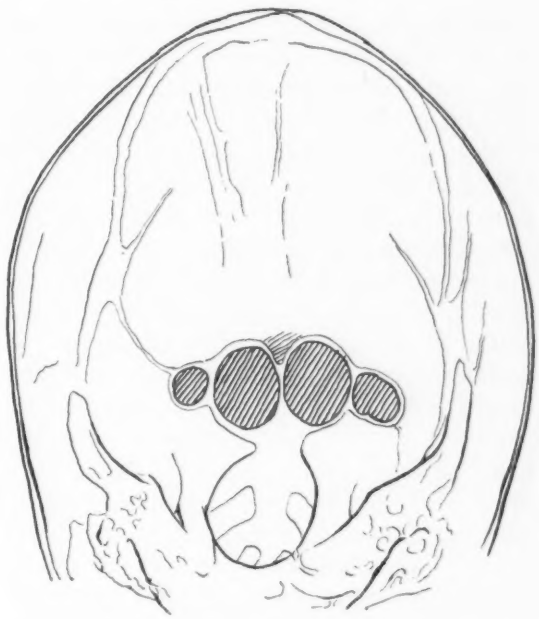


Fig. 9. Case 14. Tracings of roentgenograms in Towne projection made on the 17th day of life. Two pairs of oval ossicles, one larger medial pair and one smaller lateral pair, are visible in the innominate synchondrosis. A short Kerkring-like process lies between the upper poles of the medial pair of ossicles.

### REVIEW OF FINDINGS IN 15 CASES

*Prevalence of Ossicles.* In this series of 3,800 newborn infants, supraoccipital ossicles were found in 15, or 0.4 per cent. This figure is probably much too low. In lateral projection, which was used alone routinely in this series, small bones in the innominate synchondrosis can easily be overlooked, because the small shadows of the ossicles are superimposed on the heavier shadows of neighboring bones, whenever the head is even slightly rotated or tipped off its full lateral projection. Undoubtedly the use of the Towne projection as a routine would have increased the incidence substantially.

*Number and Size.* At birth, one to four ossicles were present in each case. They varied in greatest diameter from 20 to 5 mm. during the neonatal period. The largest ossicles were found in cases in which three or more ossicles were present (Cases 12, 13, 14, and 15). With one exception (Case 13), the more medially placed ossicles were the largest. The pronounced difference in the size of the ossicles at birth suggested that the larger ones had appeared earlier during prenatal life or had grown more rapidly.

*Location.* All of the ossicles were situated in the cartilaginous plate between the supraoccipital and exoccipital bones, directly behind the foramen magnum. Most of them were near the mid-sagittal plane of the head. Exceptions to this rule are seen in Cases 10 and 12, in which paired ossicles were situated far out in the lateral segments of the innominate synchondrosis when its medial segments contained no ossicles. Early during the first weeks of life, the ossicles were always nearer to the lower edge of the supraoccipital bone than to the upper edges of the exoccipitals. Another consistent feature in their position was the tendency for the ossicles to protrude externally beyond the outer surface of the supraoccipital; in one case (Case 12) this protrusion produced a large bony swelling behind the foramen magnum. We saw no evidence of internal projection of the ossicles—a differential feature in comparison with Kerkring's bone, which is characteristically a caudal extension of the internal table of the supraoccipital.

*Shape.* During the neonatal period, all of the ossicles save the one in Case 2 were round or oval. Their edges were all sharply defined. In density and texture, the ossicles were identical with the supraoccipital bone. In the case of the larger ossicles, there was always an indentation in the opposite edge of the supraoccipital. The depth and length of an indentation varied directly with the size of its ossicle. In some cases, the neighboring edge of the supraoccipital was thickened both internally and externally.

*Associated Kerkring's Bone or Process.* Midline shadows suggestive of Kerkring's process were found in Cases 1, 8, 9, 12, 13, and 14. These shadows fused with their medially placed contiguous ossicles during the early months of life. In Case 12, a new midline ossicle appeared on the edge of the foramen magnum between the lower poles of round paired ossicles at three months, after fusion of the neonatal midline ossicle with their upper poles.

*Course.* In all cases which were followed after the neonatal period, the ossicles increased in size with advancing age, and later fused with the edge of the supraoccipital and with one another. In no case did an ossicle fuse first with the exoccipitals. Union of an ossicle with the supraoccipital always began on its medial edge near its upper pole. When two medially placed ossicles blended, their dorsal medial segments joined first. During growth of ossicles, the indentations opposite them in the supraoccipital deepened progressively, and the ossicles gradually buried themselves into the supraoccipital which grew down around them from behind. In Case 12, a laterally placed ossicle changed from oval shape on the twentieth day to triangular shape at six months. In the same case the medially placed ossicles became more elongated cephalocaudally in the period between the third and sixth months.

The largest external bony swelling occurred in Case 12. This became much thicker during the first six months but appeared to be thinning out during the second half of the first year.

Fusion of the ossicles with the supraoccipital and with one another was complete at one year in all patients who were examined that late. In Case 12, however, at ten months when the last examination was made, fusion was far from complete, and the large amount of cartilage persisting between the bones suggested that several months would elapse before complete union would be effected.

## COMMENT

Kerkring's bone (Fig. 10) in the innominate synchondrosis was described in 1670. This ossicle characteristically appears during the fourth and fifth fetal months and disappears a few weeks before birth by complete fusion with the supraoccipital. Kerkring's bone has rarely been found as an independent ossicle; usually it occurs as an elongated bony process attached to the under edge of the supraoccipital near the mid-sagittal plane of the head, just above the foramen magnum (Augier, Lacoste, Lucy). Owing to its resemblance to a handle, Virchow called Kerkring's ossicle the manubrium of the occipital. Usually the bony process lies on the in-

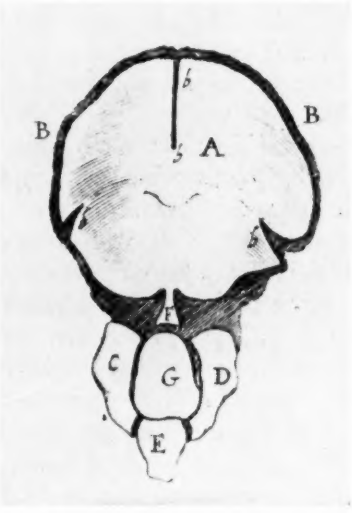



Fig. 10. Copy of the drawing of Kerkring's bone or process (F) made by Theodorus Kerkring in 1670.

ternal surface of the occipital and sometimes can be seen only from the inner aspect of this bone (Fig. 11). After birth, Kerkring's bone has apparently not been observed either anatomically or roentgenographically except in rare instances. One of our patients, six months of age, showed a shadow consistent with a large Kerkring's process (Fig. 12), and it is our impression that if Towne projections, which show the edges of the foramen magnum clearly, were made more frequently, Kerkring's bone would be found in a substantial number of infants during the first weeks and months of life, and probably later in smaller frequency. It is manifest that Kerkring's bone and process differ from the ossicles we are describing herein, in all important respects.

Accessory ossicles in the innominate synchondrosis have been recognized anatomically in but a single skull (Fig. 13), so far as we have been able to ascertain. After the dissection of the head of a newborn Russian infant, Schultz in 1917 reported paired ossicles near the lower edge of the supraoccipital similar to those in our cases. Both Weigner and Engelmann mentioned small bones in the occipital cartilage near the foramen magnum, but their descriptions are so brief that the exact nature and position of their findings are uncertain. In the comprehensive anatomical studies on the development and ossification of the cartilaginous segment of the occipital squamosa, reported by Augier and Lacoste in 1931 and 1932, accessory ossicles are not discussed.

The embryologic mechanism responsible for these ossicles is obscure. So far as one can tell, they are normal variants of developmental origin. There is no support for the idea that they are vestigial structures because they have not been found in other vertebrates or in human beings during earlier stages of fetal development (de Beer, Augier, Lacoste). The last named authors concluded that, in human fetuses, ossification in the supraoccipital begins from a single focus and develops into a single transversely elongated center which spreads by marginal growth and is not associated with secondary centers in any phase of its development. Mall did describe a quadripartite center whose different components appeared during the

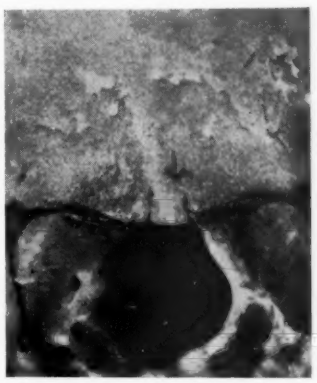


Fig. 11. Kerkring's process (arrow) in the occipital bone of a newborn Negro infant. Photograph of the internal surface of the skull. (Reproduced by permission from the original of Figure 1; Schultz, A. H. *Anat. Rec.*, 1917–1918, *12*, 358.)

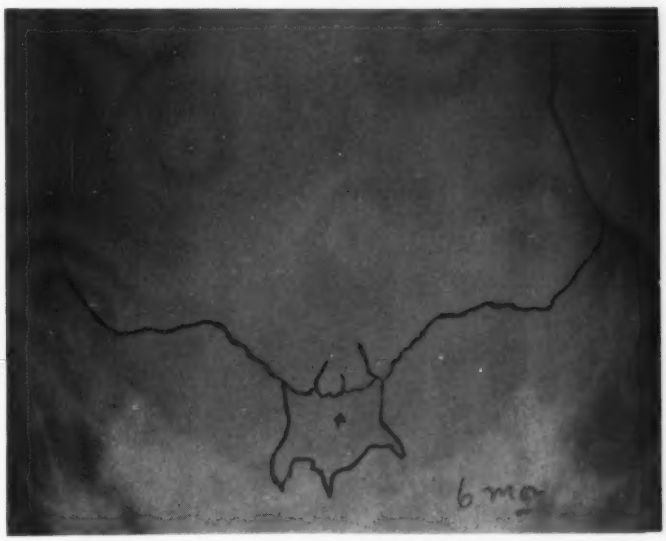



Fig. 12. Roentgen visualization of a bifid Kerkring's process (arrow) in an infant six months of age, Towne projection.

FIG. 13. Anatomical demonstration of paired round ossicles (arrows) which project externally from the innominate synchondrosis. Photograph of the external surface of the skull of a newborn infant. (Reproduced by permission from the original of Figure 2; Schultz, A. H. *Anat. Rec.*, 1917–1918, *12*, 360.)

fifty-fifth, fifty-sixth and fifty-seventh fetal days, with fusion of the four original centers into a single mass on the fifty-eighth fetal day. Mall's findings have not been confirmed in later and more adequate studies carried out with superior technical methods.

The accessory ossicles may result from excessive segmentation of the early cartilaginous occipital arch and could be the precursors of the bony thickenings, in adult skulls, on the edges of the foramen magnum which have been called "occipital vertebra" and "proatlas" by anatomists and anthropologists. The findings in Case 12, illustrated in Figure 7, are suggestive of this hypothesis of their origin.

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# FAMILIAL METAPHYSEAL DYSPLASIA*

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THIS report presents 2 cases of familial metaphyseal dysplasia which are being added to 2 already documented in the literature, making a total of 4 cases. This is probably the rarest of all the generalized diseases of bone.

The first description of this disorder was presented in 1931 by Edwin Pyle[3] in a boy, aged five. His patient showed a marked knock-knee deformity and the long bones of the arms and legs felt large and massive at their ends. The bones were not painful or tender and they functioned normally except for the presence of slight limitation, measuring about 10 degrees, in extension of the elbows. Roentgen examination disclosed a peculiar development of the bones with extreme clubbing of the metaphyseal zones. The cortex at the ends of the long bones was very thin. The architecture of the medulla and the calcium content appeared normal. An osteotomy was performed to correct the knock-knee deformity and at operation it was noted that the periosteum was normal but the bone beneath it was very soft, so that the chisel could be forced through the bone almost without use of a mallet. Bone healing appeared to be normal.

Bakwin and Krida[1] in 1937 studied the same patient described by Pyle, and at that time they again noted the slight limitation of extension at the elbows. The same deformities in the long bones were noted. The vertebrae, pelvis, skull, and face appeared normal. Blood count and complete blood chemistry disclosed no unusual findings. Anthropometric measurements showed increased length of the long bones but the sitting height was normal.

Bakwin and Krida also examined the patient's sister, and again the same peculiarity was noted in the long bones. Her blood chemistry and blood count were normal. Anthropometric measurements also showed unusual length of the extremities with a normal sitting height. They concluded that the occurrence of the same condition in siblings was an indication that the condition was familial. The parents were normal and there was no history of any bone disturbance in any of the relatives. The condition was not progressive, and did not interfere with the general health of the individuals.

## REPORT OF CASES

CASE I. Our first patient was a male office worker, aged thirty-three, who presented himself because of intermittent pain in his right ankle of several weeks' duration. The pain was more noticeable upon prolonged use of the right leg, as in standing and walking.

The past history, as given by the patient, indicated the occurrence of several pathological fractures in childhood involving the lower extremities. He could not remember the exact location of the fractures, but he stated that they healed readily without complication.

Clinical examination revealed an obvious deformity of the long bones of the extremities consisting of marked widening of the metaphyseal portions of the long bones and posterior bowing of the legs below the knees. The extremities were longer than usual but the sitting height was normal. There was slight limitation of extension at both elbows equivalent to 10 degrees of restriction.

Laboratory data showed the following: hemoglobin, 13 gm. per 100 ml.; red blood cell count, 4.5 million; color index, 0.93; white blood cell count, 8,700; polymorphonuclears, 68 per cent; lymphocytes, 29 per cent; monocytes, 3 per cent. Blood chemistry disclosed a total protein of 6.6 gm. per 100 cc.; albumin 4.2 gm. and globulin 2.4 gm. The AG ratio was 1.8:1; cholesterol was 154 mg.; calcium was 10.4 mg.; phosphorus was 3.3 mg.; alkaline phosphatase 4.5 King Armstrong units; urea nitrogen was 17 mg. Urinalysis was entirely normal.

The entire skeleton was roentgenographed

* Presented at the Fourth Inter-American Congress of Radiology, Mexico City, November 2–8, 1952.

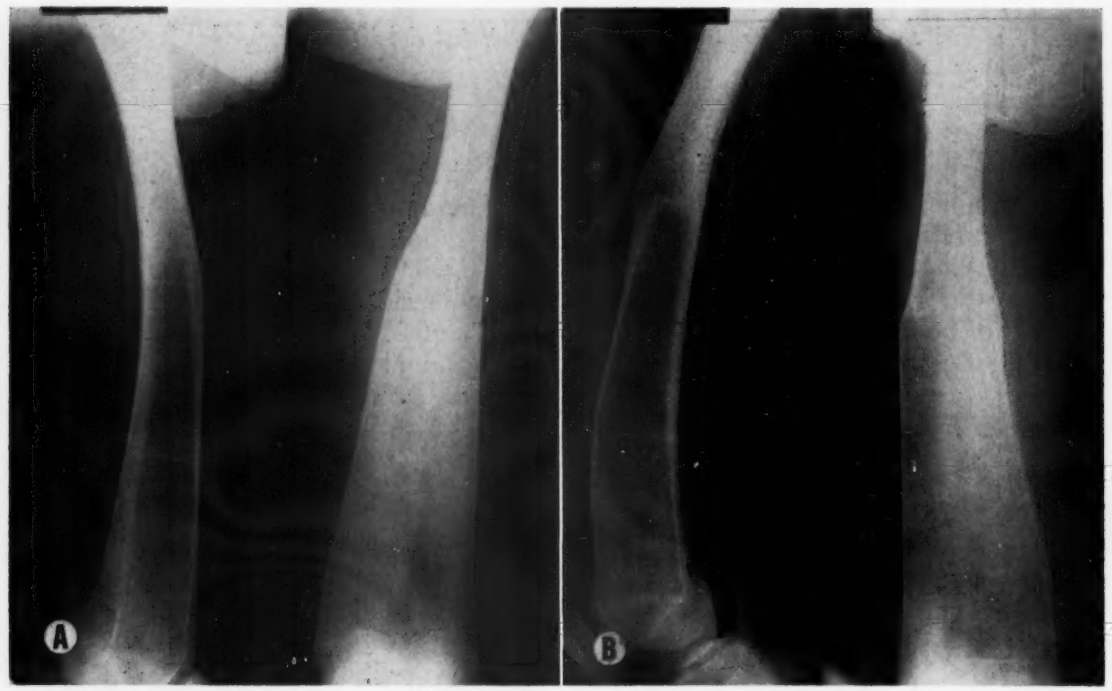


FIG. 1. Case 1. (*A*) Anteroposterior and lateral views of right femur. (*B*) Anteroposterior and lateral views of left femur. Note wide metaphyses, increased length of bones, thin cortex, transverse lines, and healed fracture in mid-shaft of left femur.

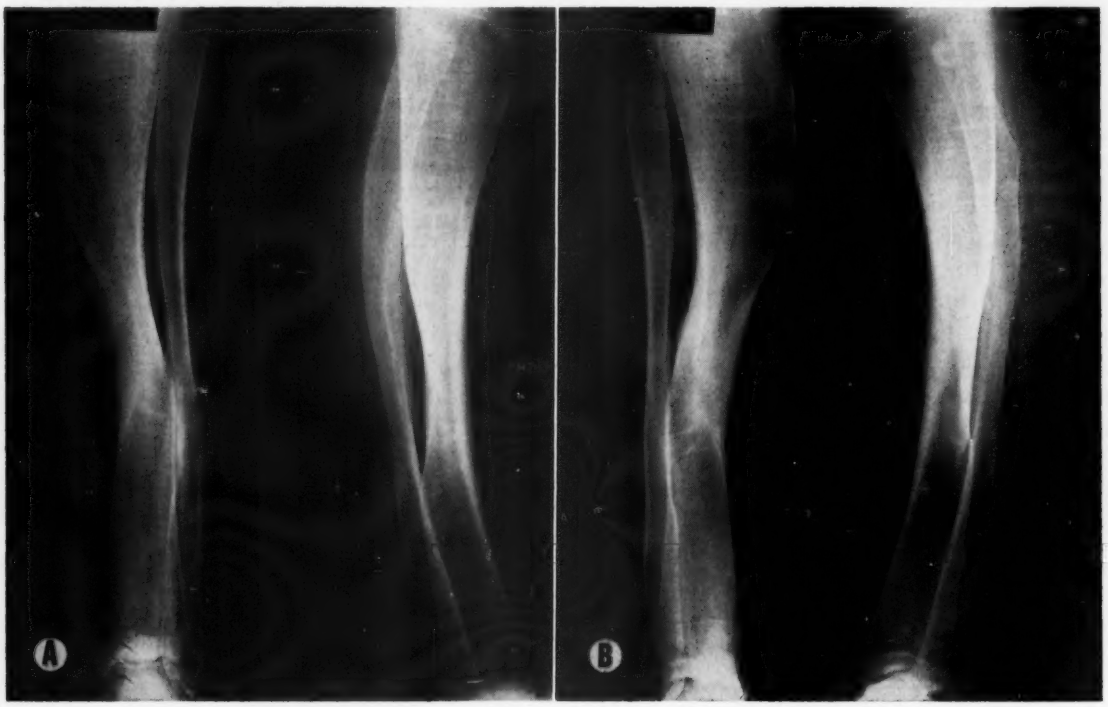


FIG. 2. Case 1. (*A*) Anteroposterior and lateral views of right leg. (*B*) Anteroposterior and lateral views of left leg. Note peculiar S-shaped appearance of the tibias in the anteroposterior projection. Probable healed fractures are evident in the mid-shafts of both tibias and in the upper fourth of the left fibula. Note also the posterior bowing of both legs.

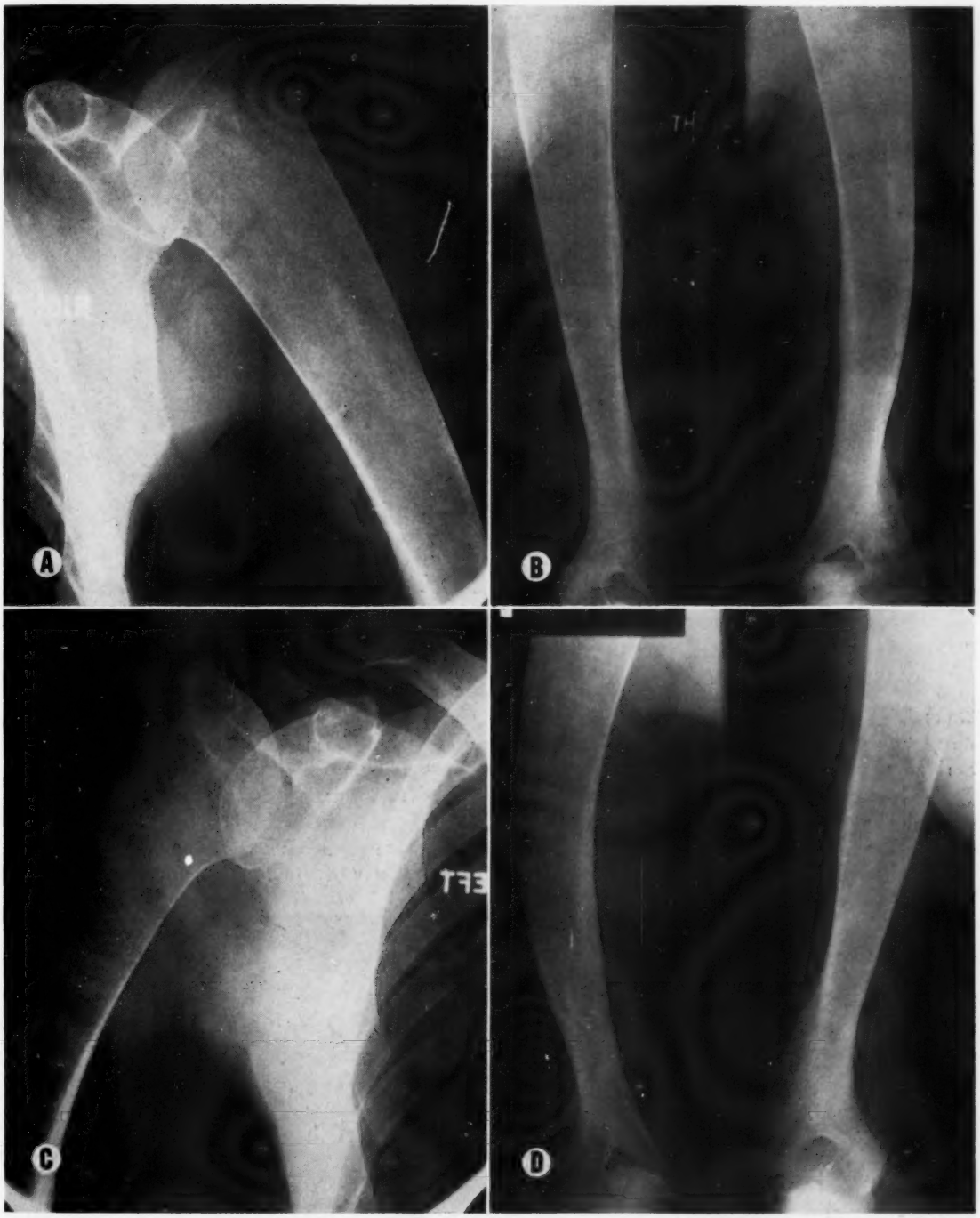


Fig. 3. Case 1. (*A*) Anteroposterior view of upper half of right humerus. (*B*) Anteroposterior and lateral views of lower half of right humerus. (*C*) Anteroposterior view of upper half of left humerus. (*D*) Anteroposterior and lateral views of lower half of left humerus. Note the lateral bowing, the increased length and the wide metaphyses of these bones.

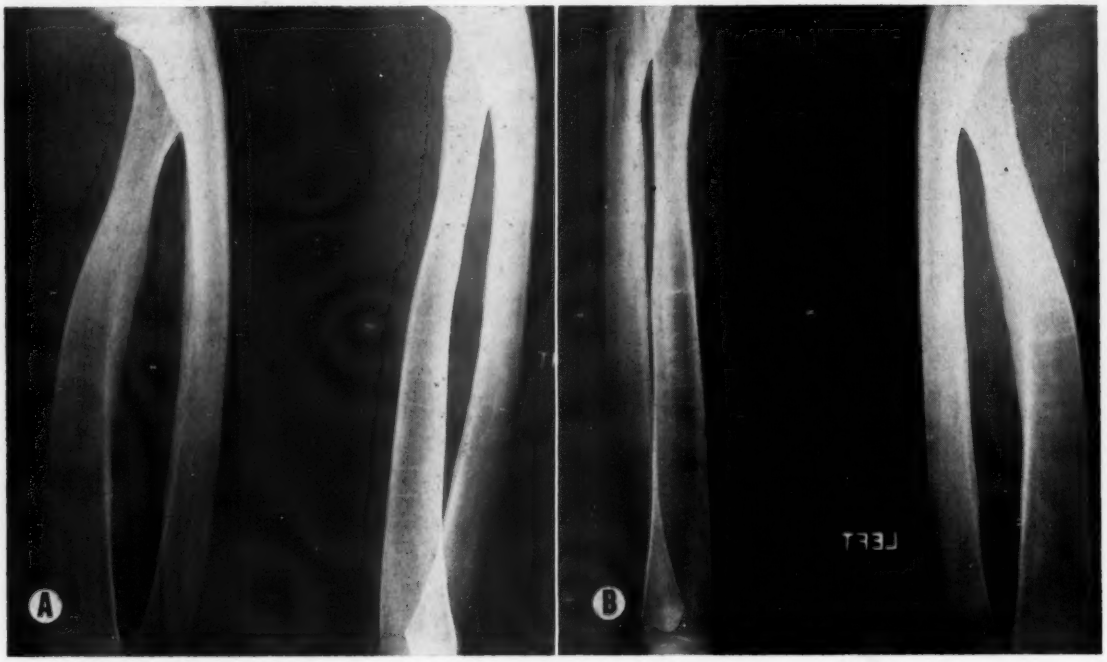

Fig. 4. Case 1. (*A*) Anteroposterior and lateral views of right forearm. (*B*) Anteroposterior and lateral views of left forearm, again showing the characteristic abnormalities seen in this malady.

and the following deformities were noted:

(1) There was an extreme widening of the metaphyseal areas of the long bones, causing a curious wine-bottle-like deformity.

(2) The long bones were longer than normal.

(3) The cortex of the long bones was markedly thinned in the metaphyseal areas.

(4) The mid-diaphyseal portion of the long bones tended toward a normal width and showed a tendency toward a cortical thickness approaching normal.

(5) The long bones, particularly those of the lower extremities, showed some evidence of malacia as indicated by posterior bowing and a peculiar S-shaped curvature in the tibias. The malacia of the bones of the lower extremi-

FIG. 5. Case 1. (*A*) Both hands. (*B*) Both feet. Note involvement of all the long bones, including all the phalanges. The carpal bones are normal in appearance.

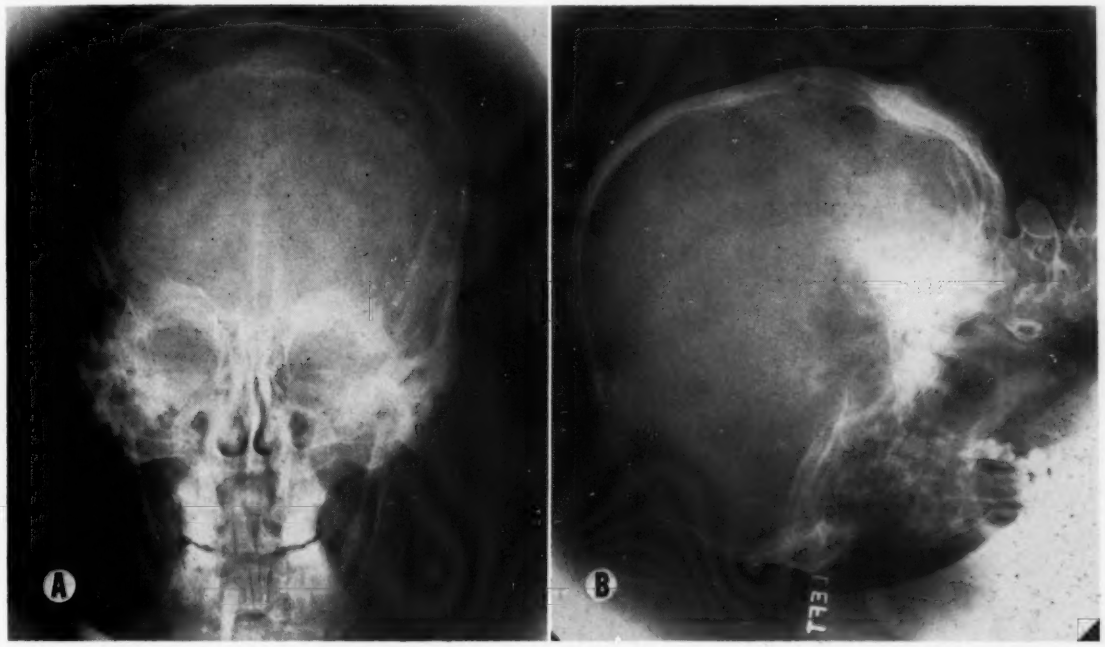

Fig. 6. Case 1. (*A*) Posteroanterior view of the skull. (*B*) Lateral view of skull. The frontal sinuses are rudimentary. A tiny ethmoidal cell is seen on the left side. The other sinuses are undeveloped. The temporal bones are not pneumatized.

ties was also indicated by evidence of healed fractures in the mid left femur, the mid portion of both tibias, and the upper fourth of the left fibula. Healed fractures were also visible in the anterior axillary portions of the fourth, fifth and sixth ribs bilaterally, and in the posterior axillary portion of the eighth left rib.

(6) Very prominent and numerous growth lines were visible in the long bones of the thighs, legs, and forearms.

(7) The temporal bones, including the mastoid processes, were not pneumatized, nor was there evidence of pneumatization of any of the paranasal sinuses except for vestigial maxillary and anterior ethmoidal cells.

(8) The flat bones were not peculiar but the anterior ends of the ribs showed evidence of flaring.

The patient's family was investigated as extensively as possible. Two children of the patient, a girl aged five and a boy aged fifteen months, showed no evidence of bone disease. The patient's parents were normal. However, the patient's sister was afflicted with the same malady, and the findings are as follows:

Case II. This patient is the older sister of the patient described above. She is thirty-four years of age and works as a medical technician. She was completely unaware of any bony abnormality, and she never had any symptoms. She had no evidence of limitation of extension at the elbows which was noted in the other 2 cases. Twenty-six years ago she was in an automobile accident in which she sustained several fractures in her right hand. These healed without complication. In January, 1947, she was in another automobile accident which resulted in 19 rib fractures. Again these healed normally. Though roentgenograms were made after both injuries, the patient never learned of her skeletal aberration, and perhaps it was overlooked. She never had any symptoms referable to the bones and joints, and it was only as a result of our investigation of the first case that we discovered the second one. Unfortunately, the second patient lives at a great distance, and we could only contact her by mail. We could not get a complete medical and laboratory study, but we were fortunate enough to get roentgenograms of her lower extremities. These films again show the remarkable changes seen in the roentgenograms of her brother. We were unable to obtain films of the ribs to see the effect of trauma on these struc-

tures. It would have been interesting to see if the paranasal sinuses and the temporal bones were pneumatized. In spite of the fact that we could not fully study this case, the available data seem sufficiently interesting to warrant reporting.

## DISCUSSION

Though the morbid process in this disorder remains obscure, apparently some disturbance of the factor which controls modeling of the long bones is present. This error in tubulation accounts for the marked flaring of the metaphyses, the extremely thin cortex, and the increased length of the long bones. Since tubulation is thought to be a function of the metaphyses, it is probable that this disease is a primary dysplasia of the metaphyseal ends of all the

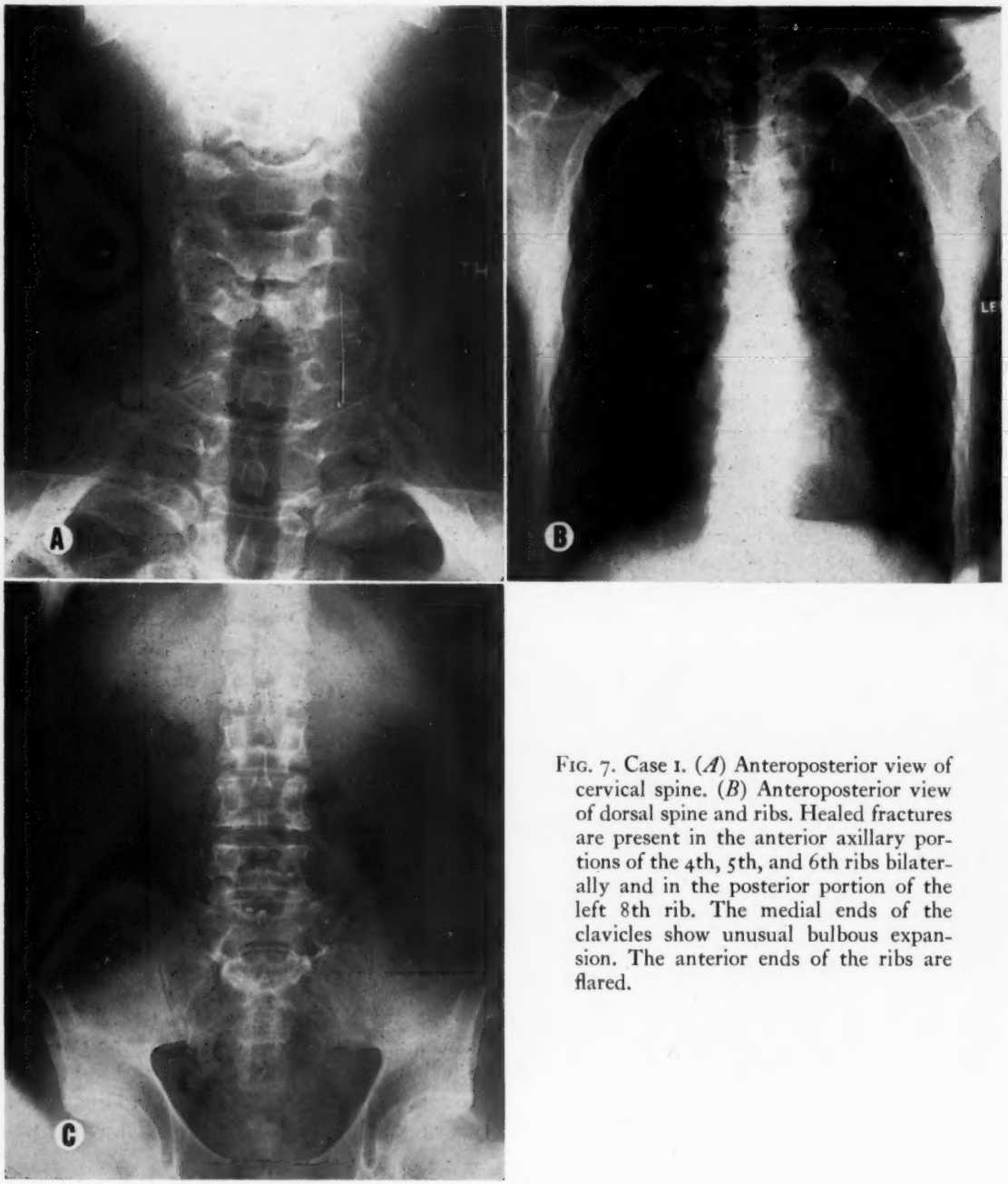


FIG. 7. Case 1. (*A*) Anteroposterior view of cervical spine. (*B*) Anteroposterior view of dorsal spine and ribs. Healed fractures are present in the anterior axillary portions of the 4th, 5th, and 6th ribs bilaterally and in the posterior portion of the left 8th rib. The medial ends of the clavicles show unusual bulbous expansion. The anterior ends of the ribs are flared.

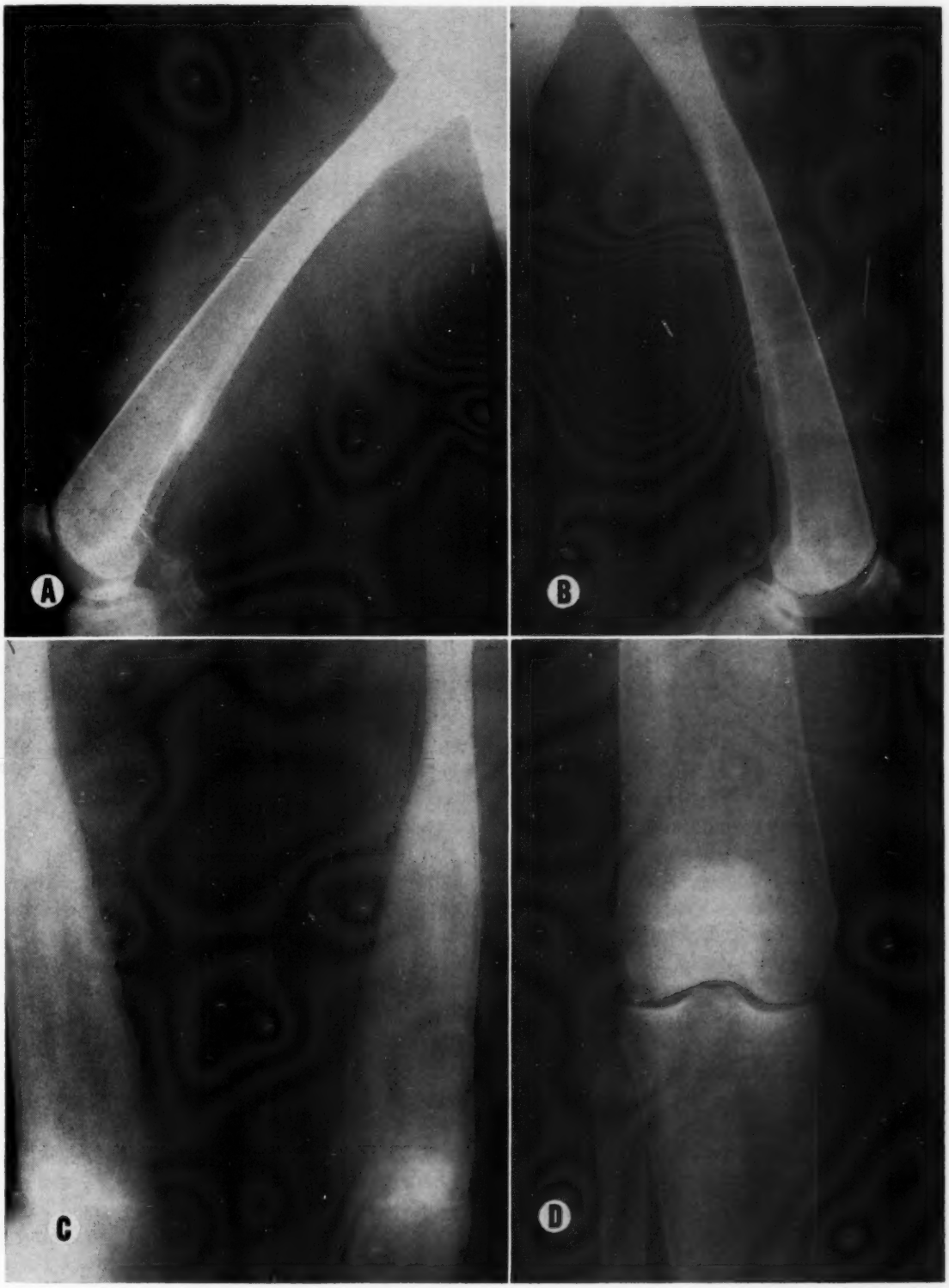


Fig. 8. Case II. (*A*) Lateral view of right femur. (*B*) Lateral view of left femur. (*C*) Anteroposterior view of the femurs. Note the remarkable similarity to the first case. No evidence of healed fracture is present. (*D*) Detail view of the left knee.

FIG. 9. Case II. (*A*) Anteroposterior view of both legs showing the same S-shaped bowing as in Case I. No healed fractures are evident. (*B*) Lateral views of both legs showing the posterior bowing seen in Case I but to a lesser degree here.

long bones. This disease is remarkable because of the great number of transverse lines in the bones of the lower extremities. These cases refute the idea that transverse lines result solely from arrested growth, since in the present case the bones displaying the most transverse lines reveal the most excessive growth. This is in accord with Caffey's[2] findings of transverse lines developing in sites of accelerated growth. It is more likely that transverse lines are a manifestation of disordered growth, rather than a manifestation of arrested or accelerated growth.

The marked thinning of the cortex presumably results in some degree of osteomalacia as indicated by the numerous pathological fractures which occurred in the first case, though pathological fractures were not present in the cases of Bakwin and Krida. They, as well as Pyle, however, noted knock-knee deformity in the 2 cases reported earlier.

The absence of pneumatization of the temporal bones and the almost complete failure in development of the paranasal sinuses were not noted by Krida and Bakwin in their cases. The significance of these findings is not understood.

## DIFFERENTIAL DIAGNOSIS

Though under-constriction of the bones occurs in many conditions, including diseases which infiltrate the bone marrow, such as leukemia, Gaucher's disease, erythroblastic anemias, deficiency diseases such as healing rickets, healing scurvy, cystic fibrosis of the pancreas and developmental diseases such as chondrodystrophy and osteopetrosis, the findings in familial metaphyseal dysplasia are so characteristic that they cannot be confused with any of the above-mentioned entities.

Engelmann's disease, of which 9 cases have been reported, is characterized by hyperostosis of the diaphyses producing fusiform widening of the mid-shafts of the long bones. In this disease the diaphyseal areas of the bones are widened, but the metaphyses have a normal configuration.

This disease, likewise of obscure origin, does not fit into the same category as metaphyseal dysplasia, inasmuch as it is associated with pain and muscular atrophy, whereas in metaphyseal dysplasia there is no involvement of the extraosseous tissues. It is noteworthy that Bakwin and Krida's cases occurred in a brother and sister, and our cases likewise are in a brother and sister. So far as can be determined, no relationship exists between their cases and ours.

## SUMMARY

Two cases of familial metaphyseal dysplasia are added to the two cases previously described in the literature. Curiously enough, the cases herein reported occurred in a brother and sister, as did the previous two cases. The outstanding clinical findings include increased length and widening of the extremities with some degree of osteomalacia. The outstanding roentgen findings include failure of tubulation of all the long bones, increased length of the long bones, widening of the metaphyseal ends of the long bones, causing a curious wine-bottle appearance, marked thinning of the bony cortex, numerous transverse lines, particularly in the bones of the lower extremities, flaring of the anterior ends of the ribs, and failure of pneumatization of the temporal bones and the paranasal sinuses.

The general health of the patient does not appear to be affected.

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# PARADOXICAL CROSSING OF THE RADIUS IN ANTEROMEDIAL DISLOCATION OF THE HEAD OF THE RADIUS TO GIVE SUPINATION CONTRACTURE OF THE FOREARM

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THE genesis of a supination contracture of the forearm lay in the paradoxical anterior crossing of the radius over the ulna by anteromedial dislocation of the head of the radius. Such a dislocation to my knowledge has not been previously described.

## REPORT OF CASE

A woman, aged thirty-seven, struck the point of her right elbow in July, 1943, when she fell from a ledge 3 feet high. Immobilized in plaster for a week, she could not thereafter straighten the joint. I saw her on November 17, 1943, at the request of Dr. Mark Youmans. The dislocated head of the radius was fixed anteromedially under the mass of muscle arising from the internal epicondyle of the humerus. Flexion of the elbow reached 70 degrees and extension 100 degrees. The forearm was fixed in supination contracture of 80 degrees. Neither the radius nor the ulna showed evidence of fracture. The hand and wrist were normal (Fig. 1, *A* and *B*).

The resection of the head and neck of the radius was attempted through an anteromedial incision on November 12, 1943. The inner border of the pronator radii teres was retracted medially, together with the median nerve. The ulnar artery crossed the neck of the radius. The yellow and decidedly frayed tendon of the biceps inserted more laterally than seemed normal. The constricted capsule overlying the dislocated head was released. An adequate resection could not be done in so cramped a space. The radius was therefore exposed through a dorsal incision. A mass of scar tissue bound the radial head firmly. This was resected to free the head and neck of the radius. It was then possible to bring the head dorsally to its normal site to effect the resection. Even then, the supination contracture persisted. On manipulation of the forearm, adhesions were heard breaking as the forearm was pronated. The forearm was immobilized by plaster in pronation and the elbow flexed.

I did not see her again until June 26, 1946. She had received physical therapy for one and a half years after operation. She had no complaints except the inability to pronate the forearm as in typing or playing cards. The contour of the elbow joint was normal. Flexion of the joint reached 70 degrees and extension 170 degrees. Supination was possible from 10 degrees to 80 degrees but there was no pronation. The forearm was slightly atrophic. Wrist motions were free. The volarly displaced ulnar head had little passive dorsovolar motion and the inferior

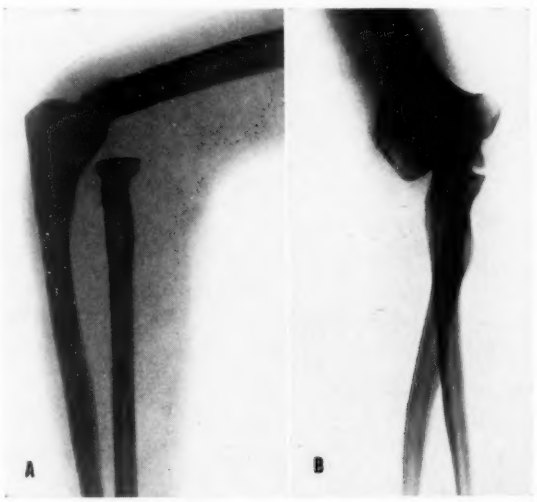


FIG. 1. (*A*) Preoperative lateral roentgenogram of the right elbow taken July 19, 1943. The radial head is dislocated anteriorly. The position of the bicipital tuberosity of the radius away from the ulna indicates supination of the forearm. (*B*) The anteroposterior roentgenogram of October 29, 1943, showing the paradoxical crossing of the ulna by the radius. The ulnar position of the bicipital tuberosity proves the forearm to be supinated.

radioulnar joint crepitated on movement of the head. The ulnar styloid was lower than the radial styloid by an apparent proximal shift of the radius. The grip was a little less than the grip of the left hand in this right handed woman. The roentgenograms taken at this time are reproduced in Figure 2.

*Comment.* The mechanics of disability which puzzled me for many years is clarified by the study of the roentgenograms which show a rotation of the *supinated* radius from the radial side of the forearm to the ulnar side, the center of rotation being the center of the inferior radioulnar joint. The radius, crossed over the ulna in paradoxical pronation, remained in the supinated position. The force pulling the radius into its abnormal position was the force of the suddenly contracted biceps muscle acting under the special circumstances of maintained flexion of the elbow and maintained supination of the forearm. Had the joint flexed, there would have been no dislocation. The force may be resolved into three components: the powerful vertical component which normally bends the elbow, an axial component approximating the radius to the humerus, and a lateral rotary component which normally supinates the forearm. The forearm was fully supinated when the dislocation took place, inactivating this component. The vertical component of force acted on a joint held in maintained flexion. The axial component played little or no part in the production of dislocation (Fig. 3).

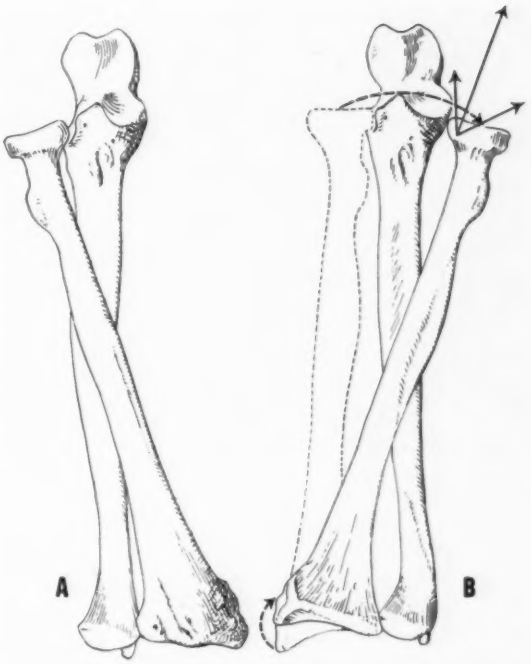


Fig. 3. Diagrams illustrating the crossing of the radius in normal pronation (*A*) and in paradoxical pronation (*B*). The direction of the radius is reversed in paradoxical pronation. The three components of force of the biceps tendon are shown. This dislocation follows the vertical pull of the biceps on an elbow held in flexion and a forearm maintained in full supination.

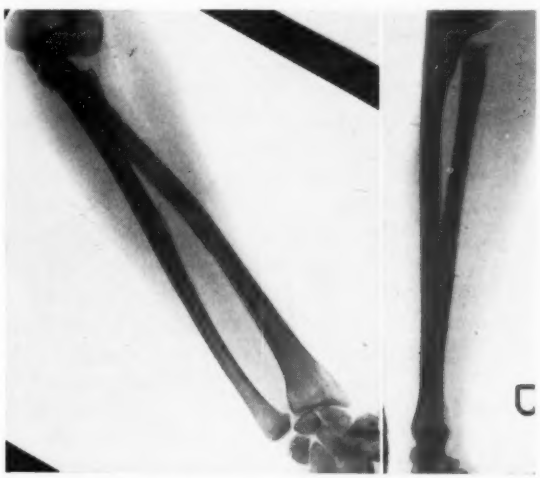


Fig. 2. The postoperative roentgenograms of June 26, 1946. The forearm is still supinated and the ulnar head is volarly placed. A radial head or pseudocaput has formed which is smooth and oblong in shape. There is a slight proximal shift of the still paradoxically crossed radius. A mild osteoarthritic change is noted in the inferior radioulnar joint.

The operation did show a change in color and change in texture of the biceps tendon and an apparent change in position of the tendon. This change in position of the biceps tendon is only apparent for in the new position of the radius it would seem more laterally placed. A great tear of the inter-

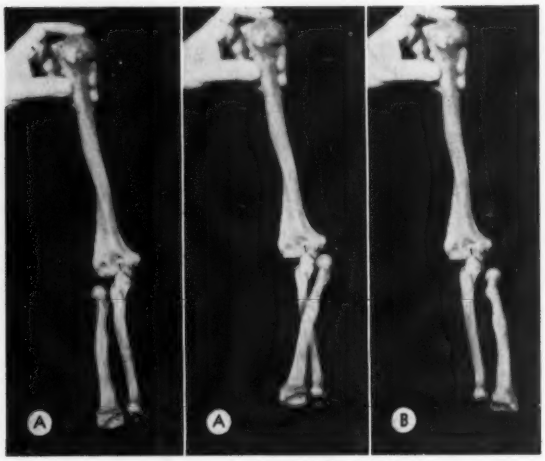


FIG. 4. (*A*) Photograph of the forearm of a skeleton to illustrate paradoxical pronation. The photograph to the left shows the position of the radius in normal supination. The photograph to the right shows the head of the radius dislocated anteromedially in paradoxical pronation. (*B*) The radius has been made to rotate to the unnatural position it occupies parallel to the ulna. It is now on the ulnar side of the ulna in a position I call paradoxical supination.

osseous membrane must have taken place to allow this paradoxical crossing of the radius.

I call this movement of the radius *paradoxical pronation* for it resembles the crossing of the radius over the ulna in normal pronation (Fig. 4*A*). Were rotation of the radius into pronation to take place from this position, the radius would have paradoxical placement on the ulnar side of the ulna, the two bones being parallel as in normal supination. One may call this *paradoxical supination* (Fig. 4*B*). The paradoxical pronation of the radius created and perpetuated the supinatory deformity of the forearm. The resection of the head and neck of the radius did not uncross the radius. The ulnar head became placed volarly as a consequence of the supination deformity and in time the inferior radio ulnar joint became osteoarthritic.

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# VOLVULUS OF THE ESOPHAGUS*

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A SEARCH of the literature fails to reveal any record of true volvulus of the esophagus. This unusual clinical entity may occur as a complication of long standing cardiospasm or achalasia.

In 1943, Williams[4] in England described the roentgenographic findings of marked esophageal dilatation in the routine postero-anterior view of the chest. His cases demonstrated appreciable encroachment on the lung fields.

Recently, Kay[2] observed a severe type of achalasia with the entire right hemithorax occupied by the esophagus.

The case to be presented verifies the findings of these authors. However, there may be the complicating factor of volvulus.

## CASE REPORT

M. B., a white female, aged fifty-one, was admitted to the emergency room of the hospital on May 25, 1951, because of severe substernal pain and dyspnea. The patient stated that the symptoms occurred suddenly one-half hour prior to admission while driving a car. On one occasion, in September, 1949, she recalled a similar but less severe episode which disappeared spontaneously. A history of a recent upper respiratory infection was elicited with some residual cough, congestion and "tightness in chest" noted on admission.

The significant physical findings were a temperature of 99.2° F., respirations 24 per minute, blood pressure 220/100, and moist rales in right posterior chest.

The clinical impression was coronary heart disease and bronchopneumonia.

Routine roentgenograms of the chest showed a well demarcated area of increased radiability occupying a large portion of the right upper lung field (Fig. 1). A narrow band of density formed the peripheral border. There was a patch-like pneumonic infiltration in the right lower lobe.

Fig. 1. Dilated air-filled esophagus contained in right hemithorax demonstrating marked encroachment on right lung. Aspiration pneumonia present in right lower lobe.

A subsequent barium swallow demonstrated a volvulus of the esophagus, with the lower two-thirds twisted on the upper third. Considerable ectasia and elongation of the esophagus was noted (Fig. 2). Some barium was seen to pass the point of obstruction.

Routine chest films obtained following roentgenoscopic examination showed absence of dilated esophagus in the right upper thorax (Fig. 3). The volvulus had spontaneously disappeared in the interim and there was dramatic relief of substernal distress. No barium, however, had entered the stomach (Fig. 4).

The patient refused admission to the hospital following the study and was advised to return at a later date.

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FIG. 2. Demonstration of volvulus by roentgenoscopic spot film. The lower two-thirds of the esophagus is twisted on the upper third.

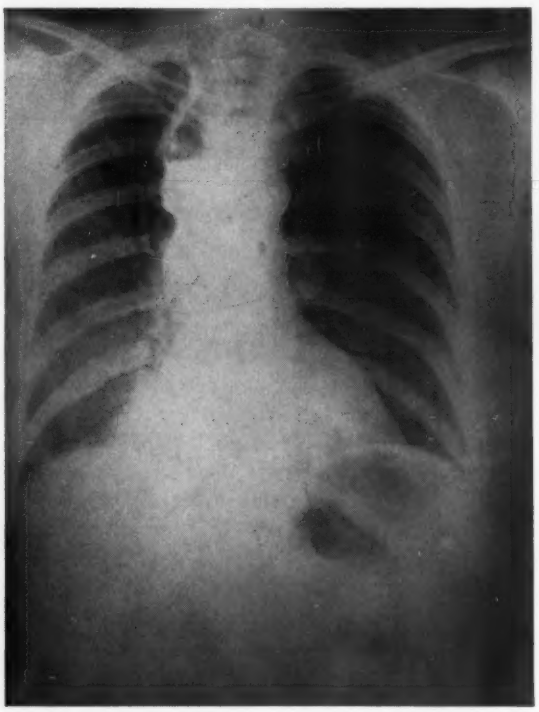

FIG. 3. Barium-filled esophagus has caused reduction of volvulus. Esophagus now lies close to midline.

In June, 1951, she was admitted to another hospital for transthoracic resection of the cardia and had a normal convalescence, but was readmitted in September, 1951, because of gastrointestinal hemorrhage. She failed to respond to conservative therapy and in November, 1951, a radical resection of the lower end of the esophagus and gastric cardia was accomplished. On the second postoperative day, the patient suffered a cerebral accident and died.

## DISCUSSION

The esophagus has three points of physiologic narrowing, namely: at the cricoid

FIG. 4. Lateral view of barium-filled ectatic esophagus.

cartilage, at the crossing of the left main bronchus and at the diaphragm.[1] The first and last of these sites are relatively fixed points. Schatzki and Simeone[3] point out that the displacement of any organ which is suspended from two more or less fixed points is necessarily accompanied by some rotation. They say, further, that twisting also occurs in this maneuver with the

torsion close to one of the fixed points.

In this instance, the volvulus occurred in a physiologic narrowed segment at the level of the arch of the aorta. Rotation occurred along the longitudinal axis with a twist of 180 degrees from left to right.

The symptomatology was easily explained by the roentgen findings in this case. The stress and strain placed upon an atonic elongated megaesophagus by the hypertonic distal portion undoubtedly was a prime factor in creating the volvulus. The production of volvulus in a redundant sigmoid or in megacolon is probably a good analogy. Reduction of the obstruction may be analogous to that observed in the colon by barium enema.

The bronchopneumonia in the right lower lobe suggests aspiration or overflow into the trachea of esophageal contents.

SUMMARY

1. A case of volvulus of the esophagus as a complication of achalasia is reported.

2. Volvulus of the esophagus is a rare entity.

3. The mechanism of volvulus of the esophagus is briefly discussed.

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# PRIMARY AMYLOIDOSIS WITH INVOLVEMENT OF THE STOMACH

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GENERALIZED amyloid deposits are not infrequently observed in association with such chronic infectious processes as tuberculosis, chronic empyema and osteomyelitis. There is, however, a much rarer form of generalized amyloidosis which is apparently unassociated with preceding or concomitant disease and which has moderately well defined clinical and pathological features. Lubarsch[14] was one of the first to direct attention to the differences between these two forms of amyloidosis, and he elaborated several criteria which when satisfied permit a differentiation between the two. These criteria quoted from Dirkse[4] and modified from Lubarsch,[14] are:

1. Almost complete absence of amyloid in organs most frequently involved in typical amyloidosis, *i.e.*, the spleen, liver and kidneys.
2. Presence of amyloid in organs and parts not usually involved; *e.g.*, the heart, lungs and skin.
3. The occasional occurrence of tumor-like nodules of amyloidosis.
4. The frequent failure of the deposits to react to the specific stains for amyloid.
5. The absence of a preceding or concomitant disease with which the presence of amyloidosis may be associated.

Cases in which the findings have fulfilled the above criteria have been designated as "primary amyloidosis," and up to 1950 Higgins and Higgins[10] were able to find only 70 instances of this condition described in the literature to which they added a case of their own. It appears that the above criteria cannot be too rigidly applied since there have been many cases recorded in which the distribution and character of the amyloid have been atypical. The most constant feature has been the absence of a preceding or concomitant disease with which the presence of amyloidosis may be associated. Although the above criteria mainly concern pathological findings, Lindsay and Knorp,[13] Eisen,[5] and Koletsky and Stecher[11] have called attention to the predominant clinical features which have at times been characteristic. For a description of cases and an elaboration of the features of this disease the reader is referred to a number of excellent reviews.[5,10,11,13]

The gastrointestinal tract has been second in frequency only to the heart as a site of involvement in this disease. In 46 autopsied cases described in the literature, Eisen[5] found involvement of the stomach in 24, or 52 per cent, and in 11 instances the deposits were extensive. Also apparently this did not include those cases in which there were only minor deposits in the blood vessels of the stomach wall. Despite this incidence, gastrointestinal signs and symptoms have only occasionally dominated the clinical picture. In only 7 cases recorded in the literature, however, there were definite signs or symptoms of involvement of the stomach. A review of the pertinent findings in these cases seems in order.

Case 1 (Steinhaus[16]). A forty year old white policeman was admitted to the hospital because of massive hematemesis and melena. No free HCl was found in the vomitus. The stomach was thought to be greatly dilated although no gastrointestinal examination was made. The heart was enlarged to percussion. The patient continued to bleed and died in about five weeks with a clinical diagnosis of a tumor of the pylorus. At autopsy the stomach was greatly dilated. The pylorus was narrowed secondarily to a marked thickening of the surrounding wall of the stomach. The mucous membrane in the region of the pylorus presented many small erosions which were the site of hemorrhage, but no discrete ulceration was noted. Microscopic examination showed that amyloid material had replaced many of the smooth muscle fibers in both the muscularis mucosae and

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outer muscular wall of the stomach. In addition, there were extensive deposits surrounding the medium sized blood vessels in the submucosa, and there was a considerable degree of necrosis of the glandular cells in the fundus and body of the stomach. The heart muscle was infiltrated with amyloid and the organ was markedly enlarged.

Case 2 (Lubarsch[14]). The patient was a white male, aged fifty-three, whose main symptoms were headache, dizziness, stiffness of the musculature of the back and extremities and difficulty in swallowing. There were also vague symptoms of indigestion. A gastrointestinal series showed no significant changes in the stomach, but there was a momentary delay in the passage of barium through the esophagus. At autopsy, in addition to widespread infiltration of the heart and skin, there was a moderate involvement of the stomach wall. The blood vessels in the submucosa were surrounded by considerable amounts of amyloid and, in addition, there was invasion and infiltration of the muscular layers. The mucous membrane presented a focal atrophy with areas of amyloid infiltration between the gastric glands.

Case 3 (Lubarsch[14]). The patient was a white male, aged forty-five, who came to the hospital because of intermittent hematemesis over a period of seven months. No free HCl was noted in the stomach, and there was a well marked secondary anemia. A gastrointestinal roentgen examination showed a narrowing of the pylorus, and because of this, a diagnosis of a carcinoma of the pyloric end of the stomach was made. The patient died following an exploratory operation, and at autopsy widespread deposits of amyloid were found in the heart, tongue, lungs and intestinal tract. There was a small tumor in the stomach wall near the pylorus. There were several eroded areas in the mucous membrane which were the site of hemorrhage. Amyloid had extensively infiltrated the stomach wall in many areas, particularly in the region near the pylorus and had thus formed a localized tumor mass. Microscopically, the amyloid was most noticeable in the region around the small blood vessels in the submucosa, but it had also replaced some of the muscle fibers in the outer muscular wall of the stomach.

Case 4 (Gottron[7]). The patient was a white female, aged forty-six, who complained of thickening and immobility of the skin over the face and body. There was also a marked decrease in intestinal motility, distention and constipation. A gastrointestinal series was interpreted as atrophy of the mucosa in the upper portion of the body and fundus of the stomach. There was diminished peristalsis of the stomach and the antral region was narrow and failed to dilate. This change was thought to be due to an infiltration of the wall of the stomach with resultant loss of mobility. Biopsies of the skin confirmed the diagnosis of amyloidosis.

Case 5 (Clausen as quoted from Heeren[2]). A gastrointestinal series showed an obstruction of the pylorus due to a tumor about 2 cm. in diameter. Proximal to the pylorus, there was strong peristaltic activity but there was marked delay in the emptying of the stomach. A diagnosis of (1) marked scarring of the stomach wall or (2) tumor was made. At autopsy fourteen days later, amyloid deposits were found in the mucous membrane of the stomach and also in the thick muscular wall of the pylorus.

Case 6 (Lindsay and Knorp[13]). The patient was a white male, aged sixty, who complained of (1) pain in the region of the thoracic spine, (2) weight loss, (3) nasal obstruction and nose bleed and (4) epigastric pain. A gastrointestinal series showed a large ulcer on the lesser curvature of the stomach. No peristaltic waves were noticed in the gastric wall in the region of the ulcer. The patient was placed on an ulcer diet, and three weeks later the ulcer was one-quarter its original size. The patient continued to suffer from a variety of symptoms, including pain in the chest, dyspnea and hemoptysis. During the remainder of the illness, symptoms referable to the gastrointestinal tract were minimal, and the patient died about eight months after the onset of his last illness from what appeared to be heart failure. At autopsy there was a large 4 by 5 cm. ulcer on the lesser curvature of the stomach. Its edges were elevated, sloping and indurated and there was almost complete perforation of the stomach wall. Microscopic examination showed that there was an extensive deposit of amyloid in the region of the ulcer. The stomach mucosa was thin and atrophic and the gastric glands were irregularly arranged and were separated by many lymphocytic collections and masses of amyloid. In addition, there were extensive deposits of amyloid in the heart, pulmonary artery, lymph nodes and bone marrow.

Case 7 (Golden[6]). The patient was a Negro female, aged sixty-six, who came to the hospital because of massive hematemesis. Diarrhea had been present for about one week before admission during which time the patient had become progressively weaker. A mass could be felt in the epigastrium and a gastric analysis showed no free HCl. A gastrointestinal series showed "a constant irregular narrowing of the pyloric antrum and a large duodenal cap 7 by 7 cm. with a 50% retention of barium at the end of 6 hours." The patient was placed on an ulcer diet but there was no response. Shortly thereafter, at surgery, a white marble-like discoloration of the stomach was noted which extended into the large and small intestines. There was also a mass on the greater curvature of the stomach in the prepyloric region which was resected with approximately three-fourths of the stomach. The specimen presented two superficial ulcers 1 cm. and 1.5 cm. in diameter. Microscopic examination showed that there was an almost continuous amyloid deposit in the outer muscular

wall which had caused atrophy and replacement of the muscle fibers. There were additional deposits in the muscularis mucosae and in the walls of the blood vessels of the submucosa. This infiltration was most pronounced near the bases of the ulcers where there was considerable surrounding fibrosis.

Following the operation, the patient did poorly and died several weeks later. At autopsy amyloid deposits were found in the heart, esophagus, large and small intestine and around many of the medium-sized and smaller arteries throughout the body.

It is evident from the above review that symptoms due to primary amyloidosis of the stomach usually fall into three categories: (1) hemorrhage from ulcerated or abraded areas which have been infiltrated by amyloid; (2) epigastric pain, and (3) the symptoms of pyloric obstruction. It is likely that complaints referable to the gastrointestinal system have often been submerged by the severity of symptoms arising from such other commonly involved areas as the heart, lungs, lymph nodes and tongue.

Upon pathological examination, the most constant finding has been an extensive deposition of amyloid in the adventitia and ambient areas of the small blood vessels of the submucosa. In addition, there has been extensive replacement of the smooth muscle in both the outer muscular wall and the muscularis mucosae. Changes in the glandular portions of the mucous membrane have been less constant, but in 4 of the reviewed cases there was evidence of atrophy of the mucosa, due principally to destruction of portions of the gastric glands. In 3 cases there was an absence of free HCl in the gastric contents. In the other cases, there were no indications that an examination of the stomach contents was made.

It can be readily understood how such changes in the stomach wall could interfere with peristalsis and motility and thus mimic a carcinoma upon gastrointestinal roentgen examination. The absence of free HCl would extend the similarity. It is of diagnostic importance that in no recorded instance was the stomach the only organ involved, and usually the involvement of other organs was sufficiently great that the disease might have been detected clinically.

## REPORT OF CASE

A white male, aged fifty-nine, was admitted to the Johns Hopkins Hospital on January 30, 1951, as a known case of amyloidosis for the purpose of evaluating the effect of ACTH on his disease.

The past history was not significant except that in 1936 the patient had received an unspecified amount of antiluetic therapy.

The present illness had apparently begun about fifteen years prior to admission, when the patient had noted swelling and recurrent infection of the eyelids which had been slowly progressive and had resulted in a considerable degree of entropion. Treatment had been of little benefit and penicillin which was used for a time was discontinued because of sensitivity.

For ten years there had been a gradual enlargement of the patient's tongue. For eight years there had been intermittent attacks of rheumatism characterized by pain upon motion of the joints with slight swelling.

For five or six years there had been general lassitude, weakness and anorexia so that for three years before admission the patient had been able to work only three days a week. During the three months before admission, there had been a 10 lb. weight loss. Also, for a period of five or six years there had been a gradual enlargement of the inguinal lymph nodes.

The patient was first admitted to the Medical Service on May 27, 1949, for diagnosis because of the unusual lesions of the eyelids and because of a generalized adenopathy.

*Physical Examination.* The skin was dry and flaky. The eyelids were boggy, brown and discolored with a considerable degree of scarring and entropion. The inside of the mouth, tongue, lips and cheek were swollen and had a whitish nodular consistency and there were rubbery nodules along the temporal arteries. There were large hard submandibular nodes. The peripheral vessels were tortuous; the radial pulses were weak, and no pulse could be felt in the dorsal pedis arteries. The tip of the spleen was just palpable and the liver edge extended to 2 cm. below the costal margin.

Biopsies were taken from the buccal mucosa, from one of the submandibular nodes and a femoral mass. Microscopic examination showed

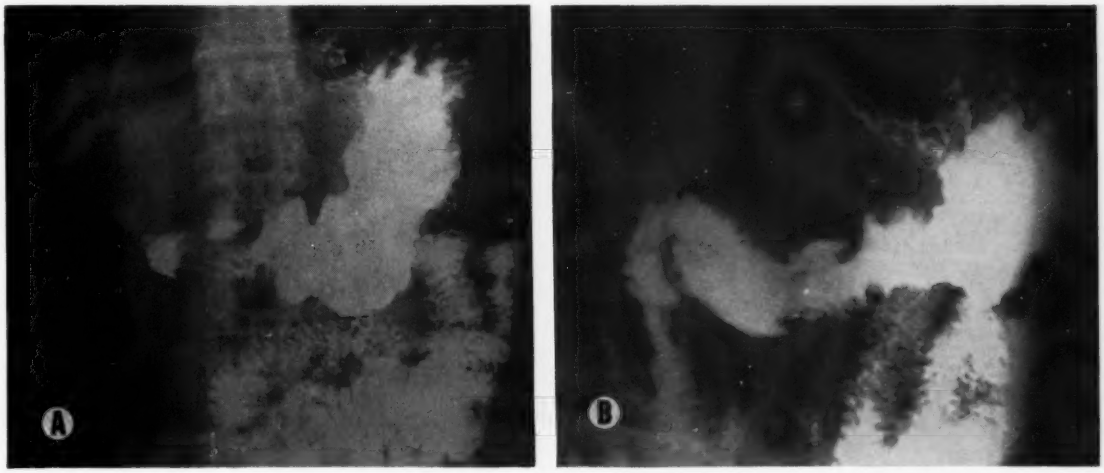

FIG. 1. Examination of March 13, 1951. Note large ulcer crater on the lesser curvature. The adjacent mucosa folds were remarkably normal in appearance. Peristalsis was sluggish in the antral region

the submandibular mass to be a salivary gland. However, confined to the adventitial areas around the large and small blood vessels there were deposits of hyaline acellular material. The inguinal mass was a necrotic lymph node. Here also all of the blood vessels showed a variable amount of hyaline-like material deposited in and around the adventitia. The lumens of several of the vessels were filled with organizing thrombi.

In the buccal mucosa the changes were quite similar but more marked. The hyaline pink-staining material, surrounding the blood vessels, formed rather large masses which accounted for the nodules which could be seen and felt clinically. This material stained pink with eosin, purple with toluidine blue, and an intense orange with congo red. The underlying muscle also stained a less intense orange color. The hyaline material was thus thought to represent amyloid and a diagnosis of amyloidosis was made.

Congo red was injected intravenously and 77 per cent was found to remain in the blood stream at the end of one hour. There was a strongly positive reaction to medium strength P.P.D. tuberculin.

A photofluorogram of the stomach on May 16, 1949, showed narrowing and irregularity of the antrum. Apparently because of the great number of other abnormalities and because there were no significant gastric symptoms, this finding was not pursued further and was forgotten until after the patient's abdomen was explored nearly two years later.

The patient was given boric acid wash for the eyes, and vitamins, and was discharged to be followed in the Medical Clinic. Symptoms remained essentially unchanged during the next twenty months although there appeared to be a gradual extension of the areas involved by the amyloid infiltration.

The patient was readmitted to the hospital on January 30, 1951, in order to determine the effects of ACTH on his disease. There were no symptoms referable to the stomach. The physical examination was similar to that described at the first hospital admission. In addition,

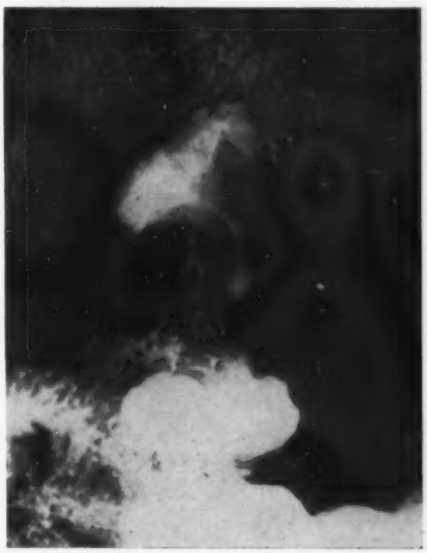

FIG. 2. Examination three weeks later. The ulcer crater appears to be slightly smaller.

there was an unusual fixed-faced expression, and the hair of the scalp, axillas and pubic region had become more sparse.

Biopsies of the buccal mucosa, left inguinal and left submaxillary regions were repeated and showed lesions typical of amyloid disease.

On the twelfth hospital day (February 10, 1951) the patient was placed on a dose of 200 mg. of ACTH daily which after fifteen days was reduced to 160 mg. daily. This dosage was continued for another two weeks. The total period during which ACTH was administered was 32 days. Immediately following the administration of the hormone, there was an improvement in appetite and a sense of well being. Later, the patient thought that the skin over the face and forehead was thinner and that perspiration over the soles of the feet was noticed where none was present before. No objective signs of improvement were noted, however.

After two weeks of treatment, postprandial pain first appeared, continued with regularity and was frequently associated with abdominal distention. Because of these symptoms the patient was given belladonna, placed on an ulcer diet, and the amount of ACTH was

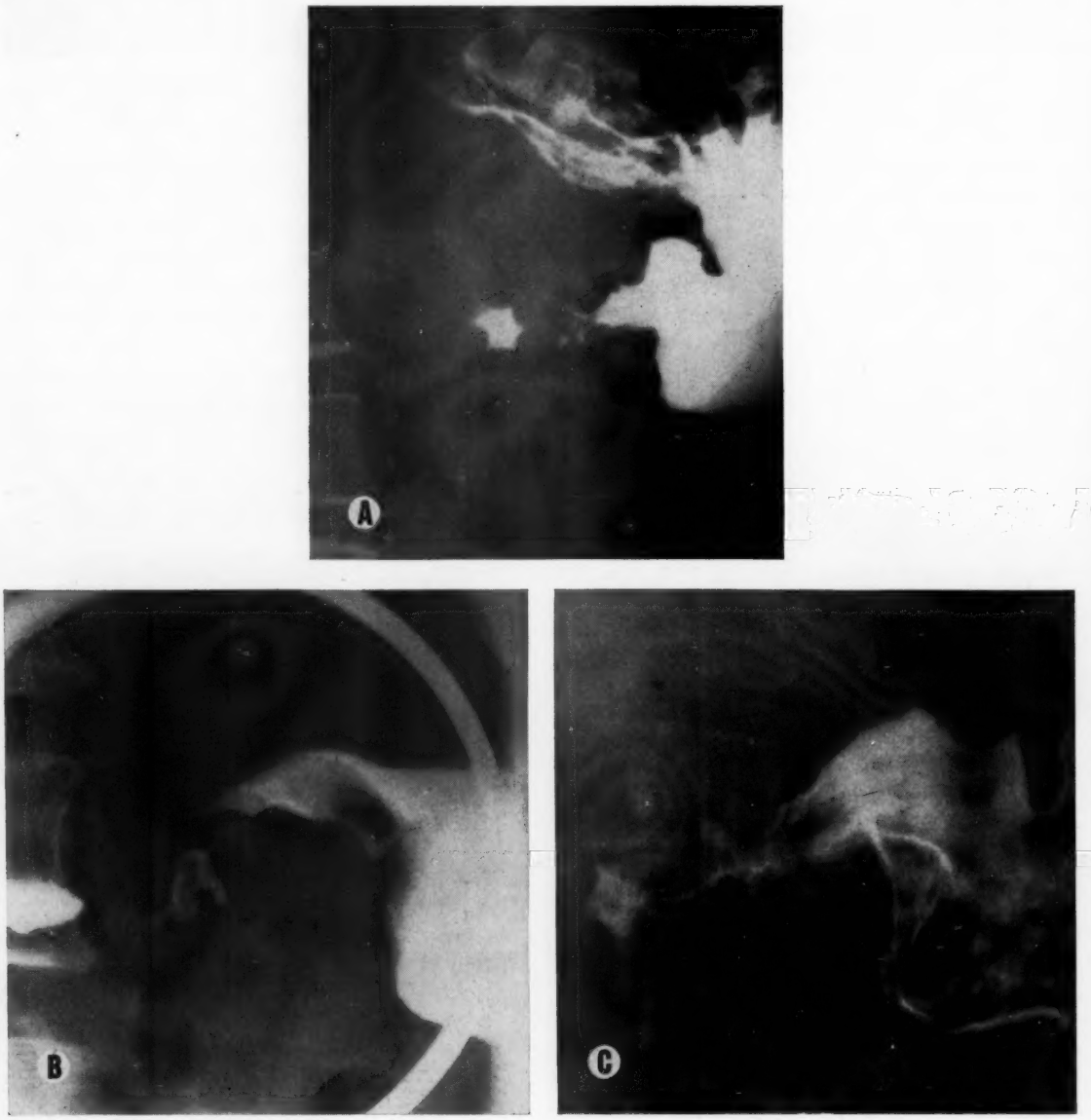


FIG. 3. Examination of April 20, 1951. The antral region shows a persistent deformity characteristic of a mass involving the antrum. An ulcer crater cannot be definitely identified.

gradually reduced. On March 13 (after 30 days of ACTH therapy) a gastrointestinal series showed a deformity of the antrum of the stomach with contraction or constriction of both the greater and lesser curvatures (Fig. 1, *A* and *B*). A large ulcer crater, 2 cm. in diameter, was apparently present on the lesser curvature. Although the antrum was narrowed, peristaltic waves passed through the area sluggishly and normal mucosal folds were present in the adjacent region of the stomach. The ulcer was thought to be associated with a mass within the stomach. The findings were bizarre but it was thought that they were due to (1) a carcinoma of the antrum with ulceration or (2) amyloid infiltration of the wall of the stomach.

Gastric analysis on March 17 (46th hospital day) showed 5° of free HCl and a 10° total of HCl. Thirty minutes following histamine, the free acid was 80° and combined 85°. On admission, no occult blood was found in the stool, but on March 16 there was a 1 plus guaiac reaction, and on the following day it was 4 plus. Following the gastrointestinal series of March 13, the administration of ACTH was stopped.

There was some symptomatic response to an ulcer diet and belladonna, although the symptoms persisted. A gastrointestinal series was repeated eight days after the initial examination and the findings were essentially unchanged. Peristaltic waves passed through the deformed antrum and this region of the stomach was more pliable than one would expect with a malignant infiltration. Again at the end of three weeks (April 6, 1951) of medical treatment another examination (Fig. 2) indicated that the ulcer crater was markedly reduced in size. The antral deformity, while still present, was less pronounced and seemed to have regressed slightly.

Epigastric pain persisted but was much less noticeable, and the stools became guaiac negative again.

A fourth gastrointestinal series, performed five weeks following the initial examination (Fig. 3, *A*, *B*, and *C*), showed a marked distortion of the antrum of the stomach. The deformity was quite constant and peristalsis was completely obliterated over a short segment of the prepyloric region. No definite ulcer crater could be demonstrated. The duodenum appeared to be normal. Most of the deformity of the antrum was thought to be due to a sizeable mass. Despite the known amyloidosis, a malignant neoplasm was considered to be sufficiently likely to warrant an exploration.

The stomach was explored (Dr. Richard Keefer) through an upper midline incision. The entire organ presented a nodular appearance with numerous thickened areas of the

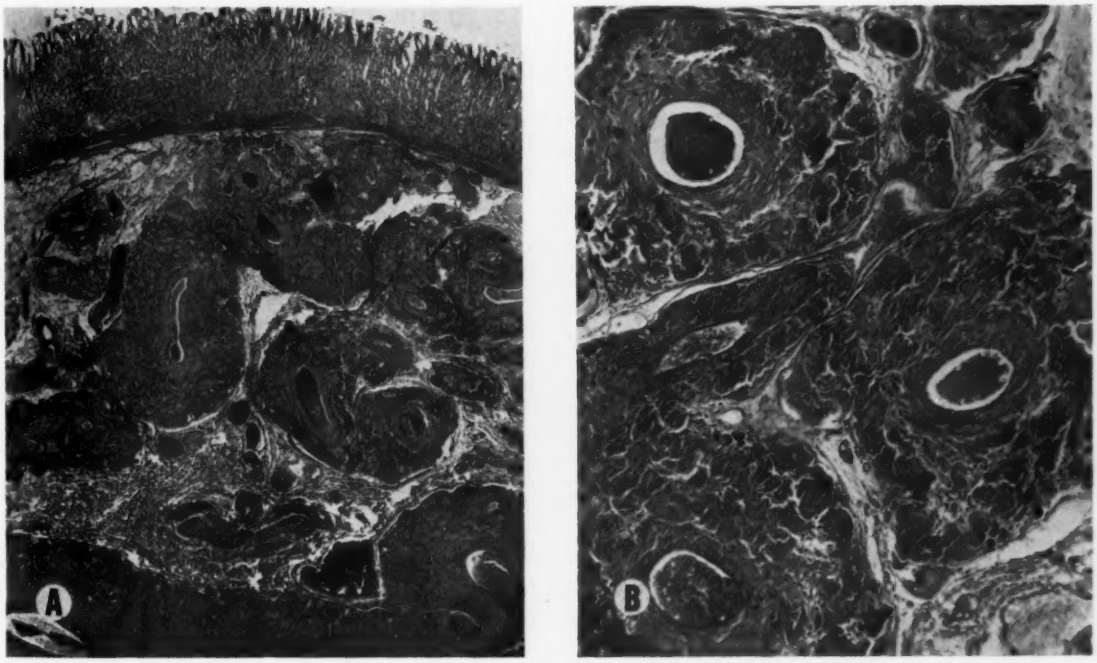


Fig. 4. (*A*) Stomach wall, ×30. (*B*) Stomach wall, ×100. Note the infiltration of amyloid around the smaller blood vessels in the submucosa.

wall; however, no localized dominant mass could be seen or felt. The stomach was opened, the interior thoroughly explored, and no evidence of ulceration was found. A biopsy specimen from one of the nodular areas in the anterior antral wall was removed as well as a section from the liver. Amyloid material was deposited in all of the major mesenteric arteries, in the wall of the small and large intestine, and there were nodular deposits scattered through the parietal peritoneum. A frozen section of the stomach showed no tumor; consequently, the stomach and abdominal cavity were closed. The patient had an uneventful convalescence and was discharged from the hospital on the ninth postoperative day.

Microscopic study of the liver biopsy showed that the architecture was well preserved and the liver cells had a normal appearance. A few medium-sized blood vessels were surrounded by large hyaline masses of eosinophilic material which was characteristic of amyloid. In the stomach biopsy the mucosa was intact and showed no lesions. Many of the blood vessels in the submucosa were surrounded by large masses of amyloid material which had not only infiltrated the muscular wall but extended into the tissue surrounding the adventitia (Fig. 4). In addition, there were a few areas where the smooth muscle was replaced by amyloid. The stomach wall was estimated to be three to four times its normal thickness.

Since discharge from the hospital, the patient had been seen several times in the Cardiac Clinic because of dyspnea and edema of the feet and ankles. The symptoms and signs indicate myocardial failure, and it is assumed that there is considerable amyloid infiltration of the heart.

## DISCUSSION

The present case is similar in many respects to the several cases previously described in the literature. In 6 of the 7 instances in which gastrointestinal series were conducted, there was narrowing of the prepyloric region of the stomach. In the seventh case (Steinhaus[16]), which was observed before the advent of the gastrointestinal roentgen ray, at autopsy the prepyloric region and pylorus were narrowed secondarily to marked thickening of the surrounding wall of the stomach. Apparently this narrowing and deformity may be due to three mechanisms: (1) the presence of a well defined mass of amyloid tissue (*i.e.*, third case described by Lubarsch[14] and Golden's[6] case); (2) a generalized thickening of the stomach wall without any localized mass (Steinhaus,[16] Clausen,[2] and Lindsay and Knorp[13]); (3) changes in motility in the prepyloric musculature without marked thickening of the stomach wall (apparently present in Gottron's[7] case). All of these mechanisms may be present in a particular case, but apparently one mechanism may often predominate. In the present case, it is thought that the deformity was due to a generalized but irregular thickening of the stomach wall.

Obstruction, associated with the narrowing in the prepyloric and pyloric areas, was noted in only 3 cases. In Steinhaus'[16] case, there was marked dilatation of the stomach with vomiting and in Golden's[6] case there was a six hour retention of the barium, and vomiting. In Clausen's[2] case, it is stated that there was a marked delay in the emptying time of the stomach. In the present case there was no evidence of obstruction. Apparently obstruction is a function of the degree of narrowing of the pylorus, although a decrease in motor activity of the stomach could be a secondary factor.

One might assume from clinical observation that amyloid has a predilection for the antral and pyloric regions of the stomach, but autopsy studies do not entirely bear this out. Records of pathological observation have not always been too detailed, but there are several instances in which it was stated that there was widespread involvement of the wall of the stomach. It seems that changes in the antral region and pylorus are more likely to produce signs and symptoms and are thus more easily detected clinically. Also, lesions in the prepyloric region are more easily demonstrated than those in the body and fundus by gastrointestinal roentgen methods. In the present instance, attention was focused almost entirely on the distal portion of the stomach and pylorus, although at operation the wall of the stomach was thought to be widely involved.

The evidence of involvement of the duodenum, particularly the first portion, cannot be accurately assessed. Clinical symptoms referable to the duodenum have not been present in any of the 6 cases in which gastrointestinal roentgen studies have demonstrated involvement of the stomach. Autopsy studies reported in the literature have not always been detailed, but infiltration of the duodenum was mentioned almost as frequently as that of the stomach. Apparently the changes did not produce many signs or symptoms and thus have not received clinical attention.

Atrophy of the gastric mucosa was thought to be present from the roentgen findings in Gottron's[7] case, but the findings of others have not been too constant in this respect. In Steinhaus'[16] case there was extensive necrosis of the glandular cells of the body and fundus, and Clausen[2] mentions an actual infiltration of the mucosa by amyloid. In 3 cases (Steinhaus, Lubarsch, Golden) multiple erosions in the prepyloric region were described. These were sufficient to produce severe hemorrhage, but from this description one would believe that they were not true peptic ulcers. In addition, they were not demonstrated by gastrointestinal roentgen examination, although it is possible that detailed mucosal studies might have revealed these eroded areas.

The present case most nearly resembles that described by Lindsay and Knorp[13] in which there was a large ulcer on the lesser curvature of the stomach. In this case there was a response by the ulcer to medical treatment but it apparently did not heal and was 4 by 5 cm. in size at autopsy six months later. The gross and microscopic description of the ulcer would lead one to believe that it was in part secondary to the large deposits of amyloid in the surrounding wall of the stomach. The edge of the ulcer was described as being "elevated, sloping and indurated" and there was a yellowish, soft gelatinous amyloid material lining the crater. In addition, the gastric mucosa was thin and atrophic. The glands were irregular and separated by amyloid. In the present case there was roentgenological evidence of an ulcer 2 cm. in diameter on the lesser curvature of the stomach. The lesion appeared to heal rapidly on a medical regimen and could not be demonstrated at operation five weeks later. This ulceration was in close relationship to an area of marked amyloid thickening of the stomach wall. There may have been some bleeding, as evidenced by the presence of occult blood in the stools. A complicating feature is that symptoms first appeared and the ulcer was first noticed while the patient was receiving sizeable doses of ACTH.

Gray *et al.*[8] have found that, following the administration of ACTH, there is an increased secretion of pepsin and hydrochloric acid into the stomach. Furthermore, patients under treatment for proved peptic ulcer had a prompt exacerbation of symptoms following the administration of the hormone, and in one case there was evidence of rapid increase in size of the ulcer with perforation. Similar observations have been made by Habif *et al.*[9] and Smyth.[15] One suspects, therefore, in the present case that a tendency to ulceration of the area of amyloid infiltration was enhanced by the administration of ACTH, and it is conceivable that it might have been the primary cause of the ulceration. The relatively high concentration of hydrochloric acid found in the present case, when compared with the absence of HCl found in other cases recorded in the literature, also suggests that the occurrence of gastric ulceration represents a response to ACTH.

It is evident that there is a marked similarity of the roentgenological manifestations of amyloid deposits in the stomach to those seen in gastric cancer. It is believed that it is impossible to differentiate between the two on roentgenological evidence alone. Minor differences which might be noted are: (1) despite evidence of rather widespread involvement, the stomach wall remains relatively more pliable and shows more peristaltic activity than is usually seen when the involvement is due to carcinoma; (2) a most important differential

feature is that there has always been definite clinical evidence of involvement of amyloidosis of some other organ or group of organs. In no case recorded in the literature to date has the amyloid deposit in the stomach been an isolated occurrence. This by no means clarifies the issue, however, since carcinoma of the stomach may occur in the presence of diffuse amyloidosis as has been observed by Bannick, Berkman and Beaver.[1]

SUMMARY

Primary amyloidosis is a rare disease which involves most frequently the heart, but in addition, often invades the stomach and the remainder of the gastrointestinal tract. Occasional involvement of the stomach may lead the symptoms which can dominate the clinical picture. A review of the literature indicates that the most frequent signs and symptoms have been hematemesis, abdominal pain and vomiting secondary to pyloric obstruction. Changes which have been found in the stomach at autopsy were: (1) infiltration of amyloid in the adventitia and ambient areas of the small blood vessels in the submucosa; (2) replacement of the portions of the muscular wall of the stomach by amyloid; (3) atrophy of the mucous membrane of the stomach which is usually extensive and associated with necrosis, degeneration of the glandular cells and infiltration of amyloid between the cells; (4) multiple erosions of the mucous membrane with hemorrhage, and (5) ulceration of the stomach wall similar to that seen in peptic ulcer. The roentgen manifestations of the changes are discussed, and their similarity to those seen in gastric carcinoma are pointed out.*

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* Since the present paper was submitted the roentgen findings in an additional case of amyloidosis of the stomach have been described by Shipps, F. C., and Brannan, D. D. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1952, *68*, 204–208.

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Vol. 70, No. 3

# SALINE CONCENTRATION IN CHOLECYSTOGRAPHY

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THE use of saline concentration during oral cholecystography has proved of great aid in demonstrating calculi when nonvisualization or poor visualization of the gallbladder has occurred.

Though oral cholecystography is an excellent diagnostic procedure for demonstrating the presence or absence of gallbladder disease, its contributions are restricted when nonvisualization of the gallbladder results. Such poor visualization may indicate hepatic or gallbladder dysfunction. The demonstration of the gallbladder with calculi will differentiate between these. We have used both laminagraphy and high dosage of the opaque medium without consistently satisfactory results. The saline concentration technique, however, has resulted in improved visualization of over 75 per cent of poorly demonstrated gallbladders with calculi.

In 1950, Cocchi reported favorably on the use of Carlsbad salts to improve the cholecystographic visualization of poorly functioning gallbladders. This report stimulated our use of saline concentration during cholecystography.

Carlsbad salts consists of 2 per cent potassium sulfate, 18 per cent sodium chloride, 36 per cent sodium carbonate and 44 per cent sodium sulfate. We have used this saline combination as well as one consisting of 80 per cent sodium sulfate and 20 per cent magnesium sulfate. Our results indicate the superiority of the latter combination.

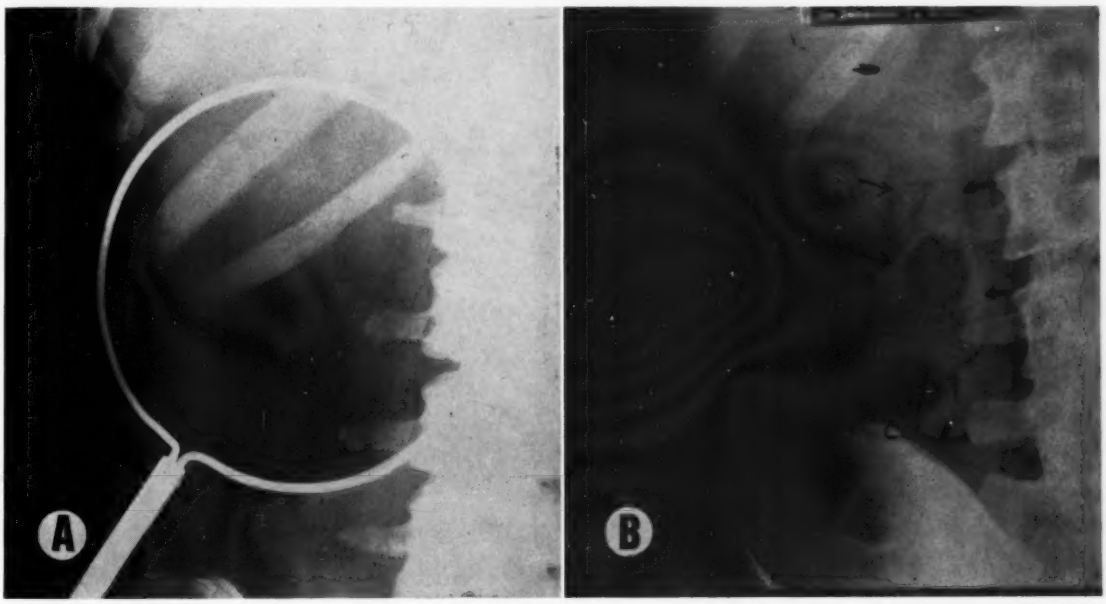


FIG. 1. Case 1. (*A*) Before saline ingestion, nonvisualization. (*B*) After saline administration. Demonstration of gallbladder and calculi.

Cocchi recommended the oral administration of one teaspoon of Carlsbad salts in 50 cc. of water when faint gallbladder visualization occurred. He administered this immediately after the first film study (thirteen to fourteen hours after ingestion of the contrast material). Ten minutes later another film study was made. Two egg yolks were then administered, followed by the last film study forty minutes later.

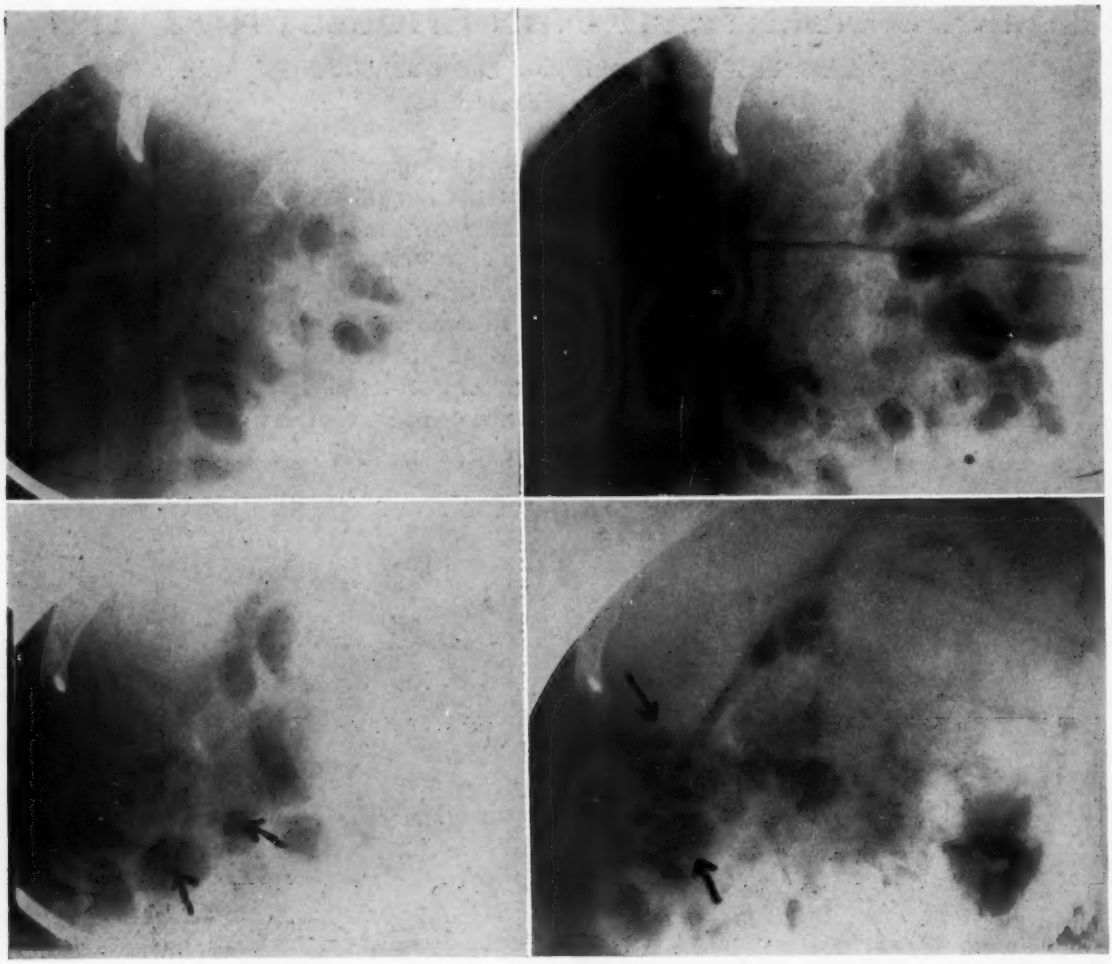

FIG. 2. Case II. *Above:* Before saline with and without compression. Nonvisualization. *Below:* After saline—visualization of gallbladder and calculi (with and without compression).

FIG. 3. Case III. Before saline, after fatty meal. Only faint visualization of gallbladder and calculi.

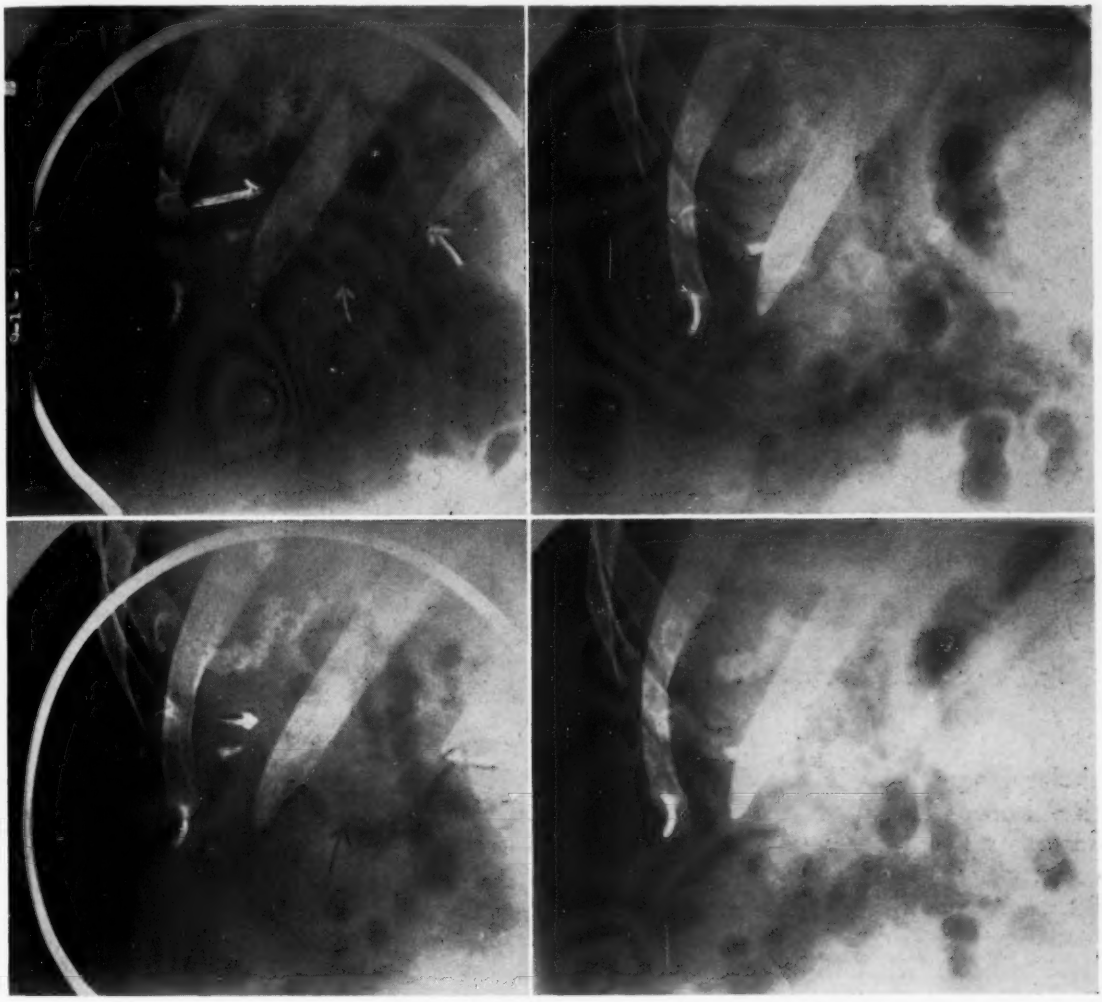

Fig. 4. Case III. After saline. Serial study with and without compression. Improved visualization of gallbladder and calculi.

We use the following procedure:

*Day before film study.*

12 Noon. Lunch. Fatty meal consisting of bacon and eggs, toast with butter, milk.

6 P.M. Dinner. Carbohydrate meal consisting of fruit juice, tomato and lettuce salad—no dressing, bread or toast—no butter, jello, tea with sugar—no cream.

6:30 P.M. 2 teaspoons of paregoric with water.

7 P.M. 1 tablet of priodax for each 20 lb. weight of the patient, or 1 capsule of monophen for each 15 lb.

Two tablets or two capsules are taken with water at fifteen minute intervals.

Thereafter only water, tea with sugar or fruit juices are drunk. Nothing else is eaten.

*Day of film study.*

Saline enema on arising.

No breakfast.

9 A.M. Report for film study.

Roentgenoscopic visualization and localization of the gallbladder area is performed, 14 to 15 hours after initial opaque medium ingestion.

Following this, sharply coned film studies of varying densities are made with and without the application of compression.

When faint visualization occurs, 1 teaspoon of saline is dissolved in 50 cc. of ice water and administered orally. The patient is informed of probable cathartic effect.

Film studies are made in erect and recumbent postures, 10 minutes, 30 minutes and 45 minutes after saline ingestion.

A lecithin fatty meal is then given and another film study made in 45 minutes.

This has proved a very valuable aid in cholecystography. In some cases, there was no visualization of the gallbladder during

FIG. 5. Case IV. Before saline. Faint visualization of calculi.

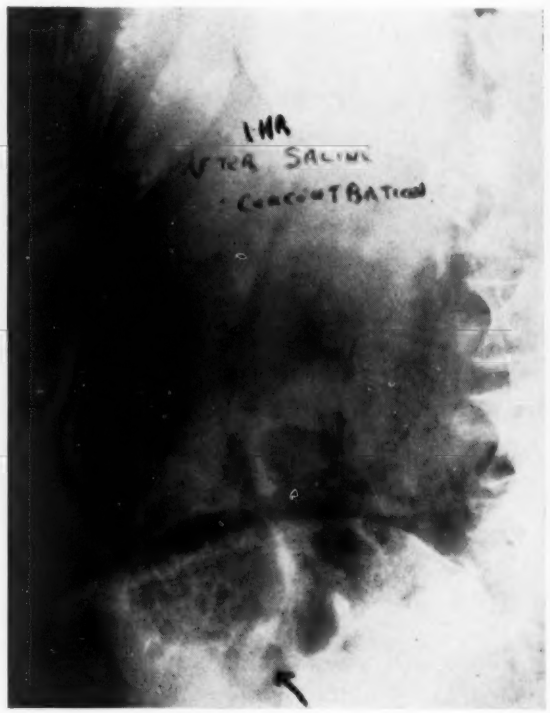

FIG. 6. Case IV. One hour after saline. Improved visualization of gallbladder and calculi.

cholecystography, while after saline ingestion both gallbladder and calculi were demonstrated (Fig. 1 and 2). In other cases, there was only faint and equivocal demonstration of poorly functioning gallbladders containing calculi, while after saline concentration, these were well visualized (Fig. 3, 4, 5 and 6).

Cocchi felt that the saline ingestion increases the tone of the gallbladder without emptying. This elevated intracystic pressure results in a marked increase in water resorption and consequent rise in concentration and density of the opaque medium. This elevated tonus and intracystic pressure without emptying following saline ingestion has been demonstrated experimentally by Brugsch and Horsters. Roentgenologically, this effect is evidenced by the reduction in width of the gallbladder which occurs in approximately two-thirds of the cases. This has been demonstrated to be a transitory change lasting five to fifteen minutes. This increased density and concentration of the opaque medium in the gallbladder may possibly be secondarily affected by further hepatic bile secretion following saline ingestion.

## SUMMARY

Oral administration of saline (80 per cent sodium sulfate, 20 per cent magnesium sulfate) during cholecystography has caused improved visualization of poorly functioning gallbladders with calculi. This improved visualization probably results primarily from a transitory rise in gallbladder tone and intracystic pressure in the absence of emptying with consequent increased water resorption. It may be secondarily affected by an increase in hepatic bile secretion.

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Vol. 70, No. 3

# RADIATION HAZARD DURING ANGIOCARDIOGRAPHY*†

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ANGIOCARDIOGRAPHY, since it involves multiple roentgenographic exposures with the injecting physician and patient in close proximity, constitutes a potential radiation hazard. There have been only a few studies of this problem.[4,6] Accordingly, we have measured the radiation received by patient and physician during angiocardiography and investigated the effectiveness of our own methods of protection.

## METHOD AND MATERIALS

Angiocardiographic technique at The New York Hospital is essentially that described by Robb and Steinberg.[2,9] The Fairchild magazine[3] is used, most patients being examined in the erect position. The arm to be injected is raised and extended anterolaterally; the one who makes the injection stands lateral to the patient, grasping the syringe along with the extended arm. The lead glass gown developed by Archer and his associates[1] is worn under the usual lead apron to afford greater protection to the injector's arms and legs. The sleeves are of three-ply construction, the remainder single-ply. Figure 1 demonstrates the patient in position as viewed from the location of the roentgen tube.

To measure the radiation in the direct beam, a Victoreen 25 r thimble chamber was used. For the smaller doses of scattered radiation, Victoreen 200 milliroentgen pocket dosimeters were used in pairs at strategic locations. The averaged readings of the paired chambers were recorded.

Initial investigation involved the placement of pocket dosimeters at appropriate locations on the body of the injector, both outside and inside the protective gown and on the hands. Measurements were made during actual angiocardiographic injections. After many trials it became apparent that results were inconsistent due to several factors. Among these were the inability to arrange all the chambers at right angles to the direction of the scattered rays and the inadvertent interposition of body parts and folds of gown between the source of scatter and the chambers. Therefore, it was decided to make measurements during simulated angiocardiography where conditions of measurement could be controlled accurately.

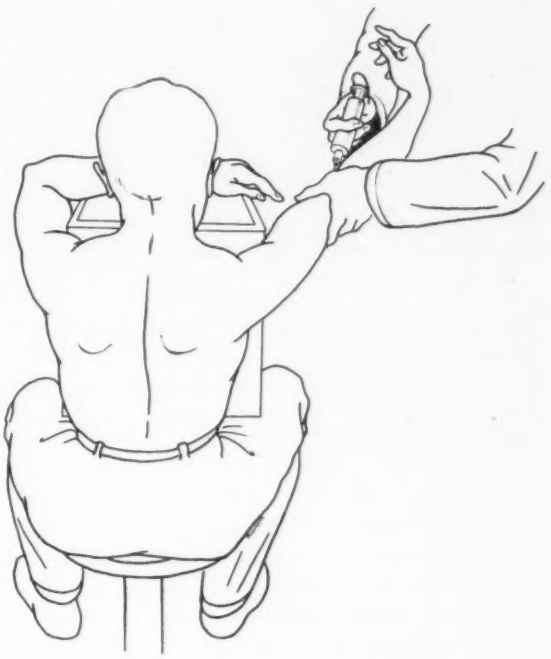

FIG. 1. Patient ready for angiocardiographic injection, positioned against the Fairchild magazine, as viewed from the position of the roentgen tube.

Subjects were positioned against the Fairchild magazine as for angiocardiography and the distance from the antecubital vein in the extended arm to the central ray was measured. A frame was then placed at this distance from the central ray and pocket dosimeters were suspended perpendicular to the estimated direction of the scattered rays (Fig. 2). These were

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† This investigation was aided by a grant from the Mallinckrodt Chemical Works and by the Bar Ray Corporation, manufacturer of the lead glass gown developed by Archer and his associates.

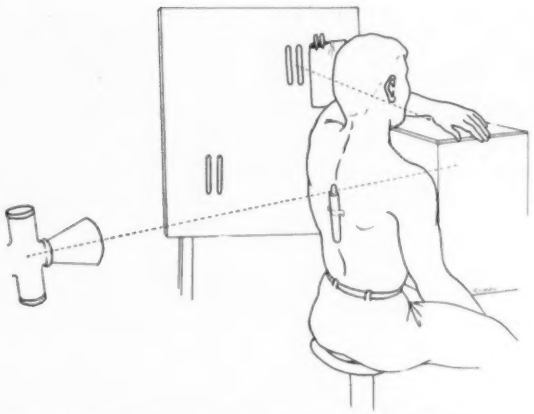

FIG. 2. Diagram of arrangement for measurement of radiation with the ionization chambers in position. See text for details.

located at (1) the calculated position of the injector's hands, and (2) at the level of the central ray. The latter position was assumed to be the area of maximum scattered radiation at the same distance from the patient as the injector's hands. In practice, the injector's body is well beyond this arbitrary point of reference. At hand level there were both unprotected chambers and chambers shielded by three-ply lead fiber glass fabric corresponding to the lead glass gown sleeves. The Victoreen 25 r thimble chamber was taped to the patient's back at the center of the field. Roentgen-ray technique was that which would be used for angiocardiography on these same patients. The target-film distance was 48 inches; 20 milliamperes and 1/10 second exposure time were used in each case. Each run consisted of ten exposures, a representative angiocardiographic series in our department. Kilovoltage ranged from 70 to 95, according to the thickness of the patient. Each series of observations included measurements with a large cone which gave a field 24.6 inches in diameter at the surface of the magazine and with a small cone which gave a field 18.3 inches in diameter.

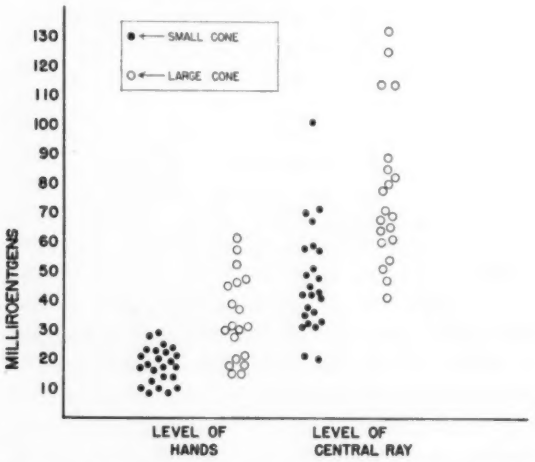


FIG. 3. Measurements of scattered radiation at the position of the injector's hands and at the level of the central ray with the use of the large and the small cones.

## RESULTS

Fifty-four simulated angiocardiograms were made with the technique as described. The results are shown as a scatter-graph in Figure 3.

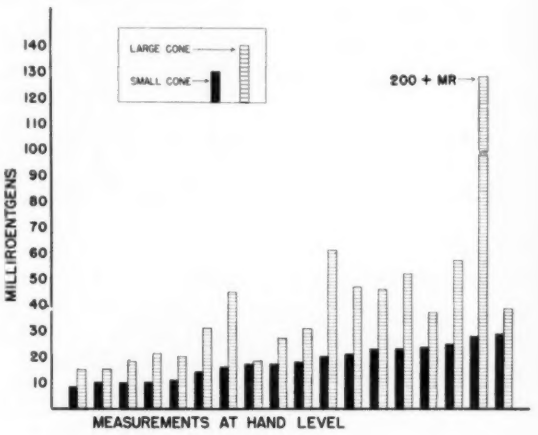


FIG. 4. Measurements of radiation dosage in the region of the injector's hands contrasting the dosage with the large and with the small cone for each patient.

Figure 4 contrasts measurements with the large and small cones at the level of the radiologist's hands. In each instance, the scattered radiation was considerably reduced by the use of the small cone. In one instance where the large cone was used and the tube was slightly off center, the dosage was disproportionately high due to the fact that the position of the injector's hands fell within the edge of the direct beam. Excluding this case, at the level of the hands the average dose with the large cone was 33 mr (range, 15 to 61 mr); with the small cone, the average was 18 mr (range, 9 to 29 mr). Exposure with the large cone

was almost twice that with the small cone.

At the level of the central ray at the same distance from the patient as the radiologist's hands, the use of the small cone resulted in similarly smaller doses of scattered radiation. Here, the average dose with the large cone was 78 mr (range, 41 to 132 mr) and the average with the small cone was 45 mr (range, 31 to 101 mr). The advantages of the smallest possible cone are evident.

The efficiency of the Archer lead glass gown in reducing the scattered radiation

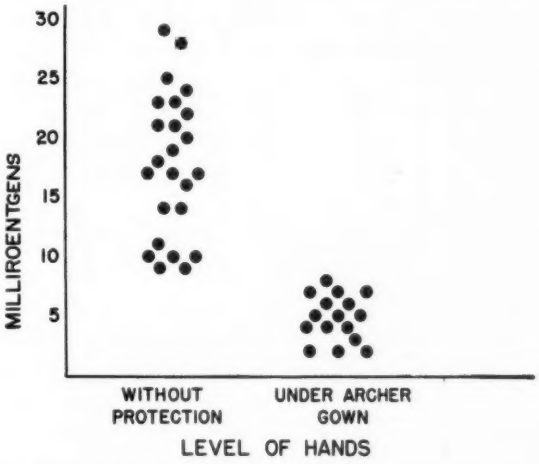


FIG. 5. Radiation dosage at the region of injector's hands with and without the protection of three-ply lead glass fabric using the small cone.

was investigated (Fig. 5). The average dose under the three-ply lead glass fabric (as in the sleeves of the gown) was 5 mr at the level of the injector's hands compared to the dose of 18 mr with unprotected chambers. Thus the amount of scatter was cut to at least one-third by the gown. It became apparent during the course of this investigation that constricting bands about the gown at the wrist were desirable in reducing the entry of scattered radiation through the otherwise open cuffs.

Radiation received by the patient at the center of the back during a ten exposure angiocardiogram ranged between 3.3 and 6.8 r with an average of 4.6 r.

Whereas, for the purposes of this investigation, ten exposures per series were utilized, it must be kept in mind that this is not always the case in clinical angiocardiography. Thus, using the small cone, the dosage per exposure received at the level of the injector's hands was approximately 2 mr and that at the patient's back was approximately 0.5 r.

## DISCUSSION

This study demonstrates that the amount of scattered radiation received by the radiologist during angiocardiography as performed at The New York Hospital is not excessive. As many as fifteen angiocardiographic injections a week may be performed before the dose at the hands reaches the weekly permissible total body dose of 300 mr as recommended by the National Committee on Radiation Protection.[8] Many more injections may be performed before 1.5 r on the hands is reached, which is the limit in this region as given by the International Commission on Radiological Protection in its recommendations.[5] However, it is always advisable to keep the radiation at a minimum, and the use of the smallest possible cone is of great value in this respect. The lead fiber glass gown is a useful adjunct in protecting the radiologist's arms, legs and back. It should never be used alone, but only in conjunction with the conventional lead rubber apron to protect the trunk. The use of cumbersome lead shields between patient and the one who makes the injection appears to be unnecessary. Similarly it is not necessary to employ artificial injection devices[7] for angiocardiography. Machines serve as a poor substitute for the hands of a skilled physician. Radiation dosage received by the patient during angiocardiography is apparently not high enough to endanger marrow or cause skin damage, but it is to be borne in mind that many patients also receive prolonged roentgenoscopy and the cumulative dosage may be high.

These results show that the procedure can be performed with safety, but it is to be re-emphasized that the above measure-

ments apply only to angiocardiography accomplished as described. This is attested to by the different values obtained by other investigators.[4,6] Angiocardiographic techniques vary greatly and therefore warrant individual assessment of the hazards involved.

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# SIMULTANEOUS BIPLANE CEREBRAL ROENTGENOGRAPHY*

*By* WILLIAM B. SEAMAN, M.D., WENDELL G. SCOTT, M.D., *and* WILLIAM D. HENRY, A.B.
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FOR complete visualization of the ventricular system following the introduction of air into the ventricles or subarachnoid space, multiple films in various positions are indispensable. Since complete filling of the ventricles is rarely, if ever, obtained, it is necessary to manipulate the head in order to move the air from one part of the ventricular system to the other. When the head is positioned with the occiput down, the air rises to fill the frontal horns and anterior half of the lateral and third ventricles. With the occiput uppermost, the air moves posteriorly and delineates the posterior portion of the lateral and third ventricles as well as the aqueduct of Sylvius and fourth ventricle. Similarly, with the right and left sides of the head uppermost, one obtains optimum visualization of the corresponding lateral ventricle and temporal horn.

Although stereoscopic views aid in obtaining a three dimensional perspective, they do not eliminate the necessity for taking roentgenograms in both frontal and lateral projections. Our routine ventriculographic examination has consisted of the following four pairs of projections: (1) anteroposterior and lateral views with the face up, (2) posteroanterior and lateral views with the face down, (3) anteroposterior and lateral views with the right side up, and (4) posteroanterior and lateral views with the left side up.

It is imperative that the head remain stationary in each position until both the frontal and lateral views are taken since any motion would disturb the position and relationships of the intracranial air shadows and make their accurate identification and localization impossible.

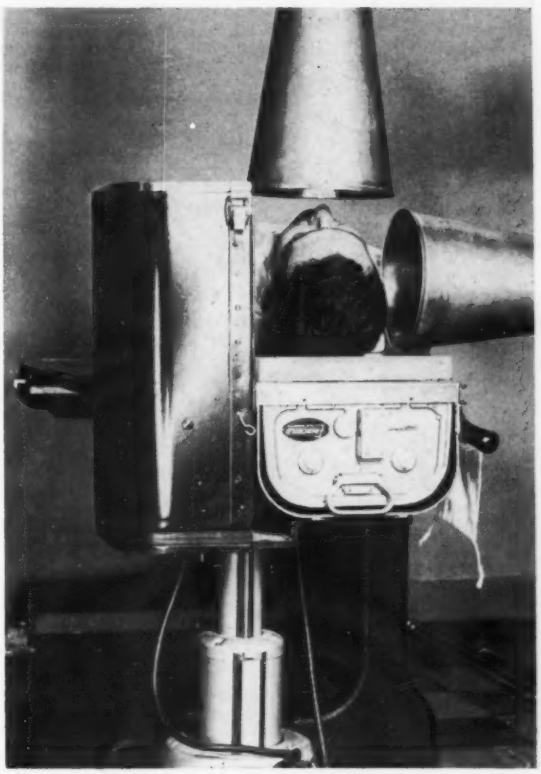

FIG. 1. Biplane roentgenographic equipment with roll film cassettes in place and patient positioned for cerebral arteriography.

In the process of modifying the biplane rapidograph designed by Scott,[1,2] it was thought that this type of equipment could also be used for ventriculography and encephalography. By exposing the frontal and lateral views simultaneously the constancy of the position of the intracranial air in the two projections would be guaranteed and the time required for the examination shortened. Accordingly, the new equipment was designed so that simultaneous right-angled projections could be taken with either conventional 10-by 12

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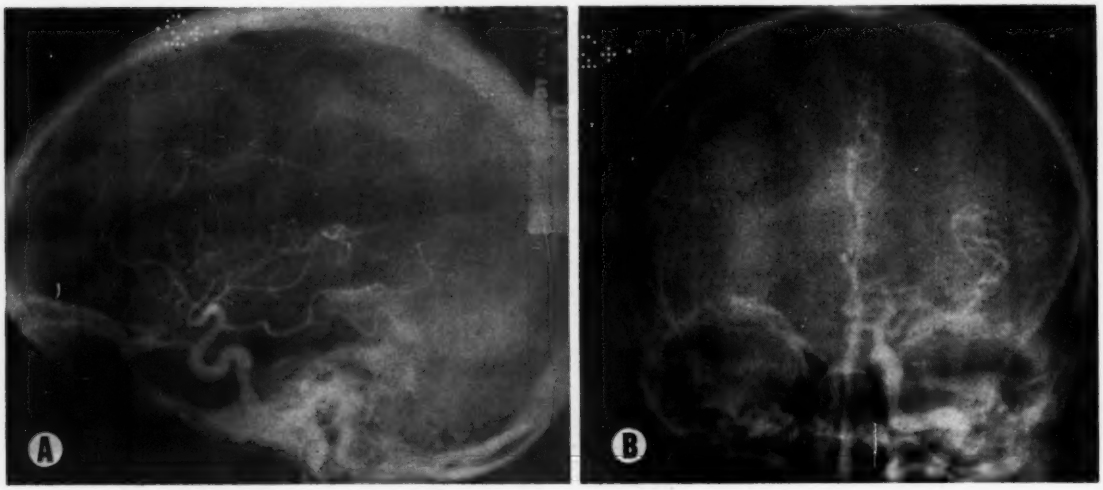


FIG. 2. Normal cerebral arteriogram. Anteroposterior (*B*) and lateral (*A*) projections were exposed simultaneously.

inch cassettes or with two Fairchild roll film cassettes for serial biplane cerebral or cardioangiography. This instrument has now been in routine clinical use for over six months and has proved to be quite satisfactory. It has diminished the time required for the examination and increased the patient's comfort by eliminating some of the manipulation.

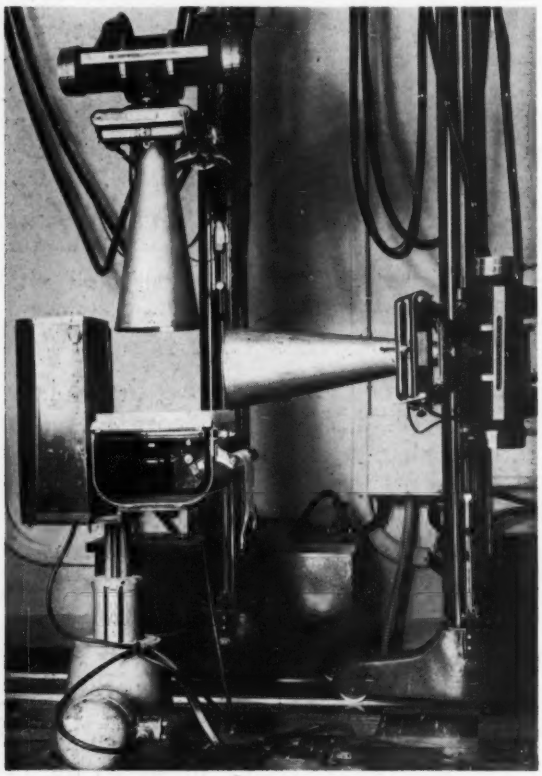

FIG. 3. Biplane roentgenographic equipment with roll film cassettes removed and adaptor inserted that permits use of 10 by 12 inch cassettes for ventriculography.

### DESCRIPTION OF EQUIPMENT

Two Fairchild roll film cassettes are mounted at right angles to each other by means of an adaptor plate bolted securely to a Ritter hydraulic pedestal base actuated by an explosion-proof motor (Fig. 1). The cassette mounted vertically is fixed, whereas the cassette mounted horizontally is adjustable so as to permit a longitudinal travel of 4 inches in either direction from a central point. This enables the use of a 40 degree tube tilt toward the feet of a supine patient while maintaining accurate centering of the skull in both anteroposterior and lateral projections. It is possible also to position the supine patient with either side of the skull next to the vertical cassette.

The Fairchild roll film cassettes can be removed from their motor frame assemblies to allow substitution of an adaptor permitting the use of conventional 10 by 12 inch cassettes, which are routinely used for ventriculography and encephalography (Fig. 3). The adaptor is slotted to receive a standard Lysholm grid. The use of an

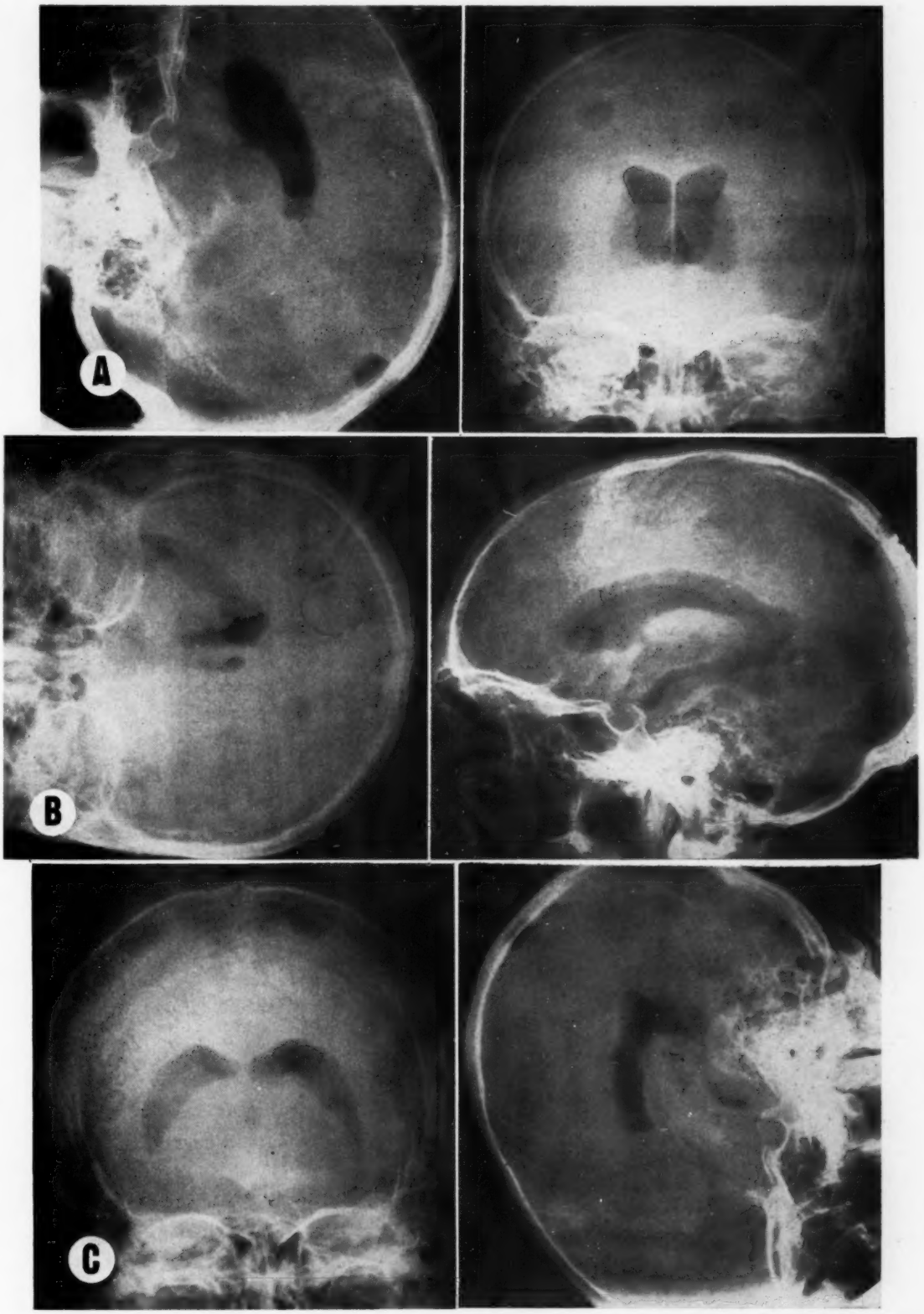


Fig. 4. The use of simultaneously exposed films in ventriculography. (*A*) Paired films taken with the occiput down. (*B*) Paired films taken with the left side up. (*C*) Paired films taken with the occiput up.

eight to one ratio linear grid gives results which compare quite favorably with those achieved with a Potter-Bucky diaphragm, while a cross-hatch grid gives even better clean-up of scattered radiation.

The pedestal base supporting the cassettes allows a vertical travel of 16 inches for positioning the cassettes to the head of the patient. The pedestal also can be rotated 180 degrees on its vertical axis allowing alternate positions for the placement of the stretcher.

The roentgen-ray equipment consists of two floor-to-ceiling tube stands moving on separate parallel tracks. The roentgen tubes are energized by two separate 300 milliampere generating systems allowing different exposure factors on each tube. The two control boards are interlocked by means of an accessory relay panel which coordinates the two electronic exposure timers with the sequencing operation of the Synchro-Trol, a component of the Fairchild equipment. Exposures are initiated simultaneously, but the relay panel prevents film advancement in either camera until the completion of the longer exposure. Provision is made for the selection of one-half, one, two, or three second intervals between successive exposures. During the course of a serial examination this interval may be changed by merely throwing a toggle switch.

Double collimation of each roentgen-ray beam is obtained by cut-out lead masks placed in the filter slots on the tube heads and on each motor frame assembly. The collimator at the filter slot restricts the beam to approximately a ½ inch clearance all around the aperture of the collimator at the motor frame assembly. The resulting collimation has proved effective in decreasing the amount of fogging from scattered radiation.

There is a 3 inch separation between the patient's head and each cassette. This is necessary for proper positioning and alignment of the skull with the film and also to eliminate fogging from the primary radiation of the beam running parallel to each film. Despite this increased film-object distance, it is still possible to obtain diagnostic roentgenograms of good contrast and definition (Fig. 2 and 4).

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The authors wish to acknowledge the cooperation and assistance of the Picker X-Ray Corporation in the design and construction of this equipment.

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# THE PATHOLOGY OF FRACTURE OF THE FEMORAL NECK FOLLOWING IRRADIATION*

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IOWA CITY, IOWA

SPONTANEOUS fracture of the femoral neck complicating irradiation of pelvic malignancy is well recognized. Although the clinical and roentgenographic features of this type of fracture are amply described by numerous writers† citing more than 100 cases, the pathologic observations are few and scattered.[1,2,4,15,18,22,23,24,25,26] Conflicting reports regarding the healing of irradiation fractures exist.[3,5,6,7,8,10,16,22,23] The unfavorable prognosis previously attached to these fractures has been partially dispelled in recent years.[3,8,10,16,22,24]

The purpose of this paper is to present the pathological changes seen in 9 of 15 patients treated for irradiation fracture of the femoral neck at the University Hospitals since the report of Stampfli and Kerr.[24] In 3 patients, specimens were obtained at the time of a vitallium mold arthroplasty. The other specimens were removed by a cannulated drill designed for biopsy of the femoral head and neck at the time of treatment of aseptic necrosis by drilling and bone grafting.[19] Unless otherwise noted, all patients received their pelvic irradiation according to the method outlined by Stampfli and Kerr which includes lateral fields. An analysis of 631 patients treated with intensive pelvic irradiation between July 1, 1943, and January 1, 1950, revealed 12 patients with irradiation fracture of the femoral neck or acetabulum. These constitute an incidence of 1.90 per cent. The revised incidence for a total of 1,983 patients treated to January 1, 1950, at the University Hospitals is 1.21 per cent.

## REPORT OF CASES

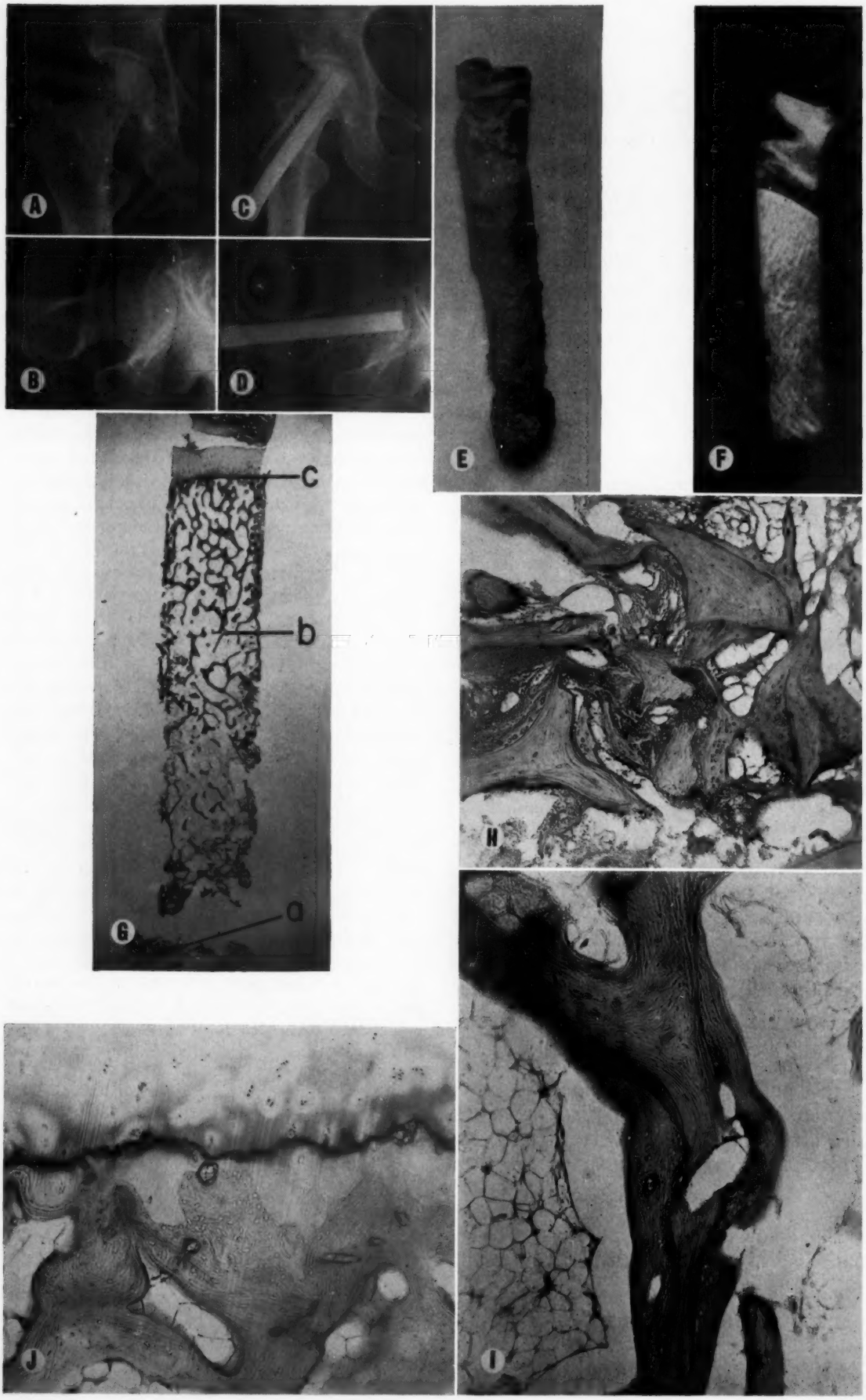
The following cases are illustrative of the pathological changes seen from four and one-half months to twelve years after pelvic irradiation.

CASE I. E. B., a woman, aged fifty-six, received 4,176 r to the midline for recurrent carcinoma of the ovary. She had had a hysterectomy and oophorectomy for carcinoma of the left ovary ten months and five months prior to pelvic irradiation. Three months after completion of therapy the patient developed spontaneous pain in the right hip and thigh. Six weeks later, roentgenograms (Fig. 1, *A* and *B*) show a fracture of the right femoral neck with slight varus deformity. There is increased density at the fracture site. The fracture was treated by insertion of a Smith-Petersen nail and intramedullary autogenous tibial bone transplant. Seven months later, bony union is present (Fig. 1, *C* and *D*). Prior to inserting the graft a biopsy 1 cm. in diameter was removed with a cannulated drill. Grossly, the area immediately below the subchondral cortex appeared white and relatively bloodless (Fig. 1*E*). The specimen roentgenogram demonstrates thinner trabeculae in the lower half (Fig. 1*F*). This trabecular atrophy proximal to the fracture site is more strikingly seen in the microscopic section (Fig. 1*G*). At the fracture site (Fig. 1*H*, area *a* in Fig. 1*G*), fibrous and bony callus surrounds necrotic trabeculae. The callus is no different from that seen in nonirradiation fractures of the femoral neck. Just proximal to the zone of osteoporosis many of the viable trabeculae (Fig. 1*I*, area *b* in Fig. 1*G*) show new bone laid on them. The lacunae in a few scattered areas of the subchondral cortex are devoid of cells (Fig. 1*J*, area *c* in Fig. 1*G*). The marrow of the femoral head is fatty for the most part. All vessels appear normal.

CASE II. H. K., a woman, aged fifty-four, was treated for an adenocarcinoma of the cervix with a tumor dose of 4,149 r and 6,160 mg. hr. of radium. Six months later, the patient had spontaneous onset of pain in the left hip and thigh accompanied by limp thereafter. Roentgenogram (Fig. 2*A*) made five months after the

† Ref. 4, 8, 9, 10, 11, 12, 13, 15, 16, 17, 18, 20, 21, 23, 24, 25.

* Presented at the Fifty-second Annual Meeting, American Roentgen Ray Society, Washington, D. C., Sept. 25–28, 1951.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onset of pain revealed a subcapital fracture of the left femoral neck without displacement. There is slight irregular mottled increase in density in the right femoral neck. The patient complained of pain in the right hip occasionally. After obtaining core biopsies, two frozen homogenous rib grafts, were inserted into the head and neck of both femurs (Fig. 2*B*, six months postoperative). The patient has had no hip pain since; however, a colostomy was performed for irradiation proctitis.

The microscopic findings on the left side are similar to those described in Case I with a few exceptions. Considerably more fibrous tissue fills the marrow about the fracture site. This is not surprising, particularly in view of the longer interval between the onset of pain and treatment of the fracture. Vascular absorption of trabeculae is especially well demonstrated (Fig. 2*C*). Some of the osteocytes in this and other trabeculae stain poorly. Many of the vessels show slight to moderate subintimal thickening but only one almost completely obliterated arteriole (Fig. 2*D*) could be found near the fracture site.

The right femoral head and neck biopsy shows partial, irregular, loss of osteocytes in the subchondral cortex, new bone laid down on old viable atrophic trabeculae (Fig. 2*E*) and no evidence of fracture. The marrow is partly fatty and partly hematopoietic. There is some increase in fibrous tissue elements in the marrow. Osteoclasts could not be demonstrated, but occasional trabeculae with osteoblasts along them were noted (Fig. 2*F*).

The most significant fact to be learned from this patient is that interruption of the circulation by fracture was not a factor in producing the changes seen in the right femoral head and neck where a fracture had not yet occurred.

Case III. M. S., a woman, aged sixty-eight, developed pain in the right hip ten months after receiving a tumor dose of 3,650 r for a carcinoma of the cervix. Roentgenograms made one month later (Fig. 3*A*) because of pain in the left hip, reveal a fracture of the left hip. Meanwhile, symptoms had subsided on the right. The patient was treated with crutches and nonweight bearing since the patient was reluctant to accept treatment by insertion of a tibial bone graft. Four months later, because of further displacement of the femoral head (Fig. 3*B*) a vitallium mold arthroplasty was performed. Roentgenograms at this time also show a segmental right acetabular fracture to account for the symptoms in that hip. The femoral head appeared normal grossly. Fibrous tissue union of the fracture was present. The capsule was thickened. No other abnormality was noted at operation. Nine months postoperatively there is healing of the right acetabulum and satisfactory progress of the left hip (Fig. 3*C*).

The microscopic section of the head (Fig. 3*D*) demonstrates normal hyaline cartilage, viable but thin trabeculae, and a fibrous tissue zone along the inferior margin. New bone is evident in this area and in sections of the femoral neck, indicating an attempt to repair the fracture. Numerous spicules of necrotic bone are within the fibrous callus. Atrophy of the subchondral cortex and surrounding viable trabeculae is apparent in a higher magnification of the head (Fig. 3*E*, area *a*; Fig. 3*D*). The marrow is mostly fatty with few areas of hematopoiesis. No osteoclasts could be found. The capsular vessels are essentially normal, except for an occasional arteriole and vein (Fig. 3*F*) with subintimal thickening. One cannot be sure, however, how much the subintimal thickening is due to irradiation damage or to the normal aging process.[14] A few cells in the vessel wall are vacuolated. A section through the acetabulum demonstrates atrophic but viable bone, for the most part. A few trabeculae show new bone on old but viable bone. However, the subchondral cortex again

Fig. 1. Case I. (*A*) (*B*) Subcapital fracture with minimal displacement four and one-half months after pelvic irradiation. (*C*) (*D*) Seven months after insertion of autogenous tibial bone graft and Smith-Petersen nail. (*E*) Gross of core biopsy, six weeks after fracture. (*F*) Roentgenogram of biopsy. (*G*) Photomicrograph of microscopic section (2×) Note zone of osteoporosis between fracture site (*a*), and middle of the femoral head (*b*). Letters indicate areas from which higher power photomicrographs were made. (*H*) Fracture site with moderate amount of fibrous and bony callus (area *a* in *G*). (*I*) New bone along old thin trabeculae (area *b* in *G*). (*J*) Normal articular cartilage. Focal area of subchondral necrosis. Fatty marrow (area *c* in *G*).

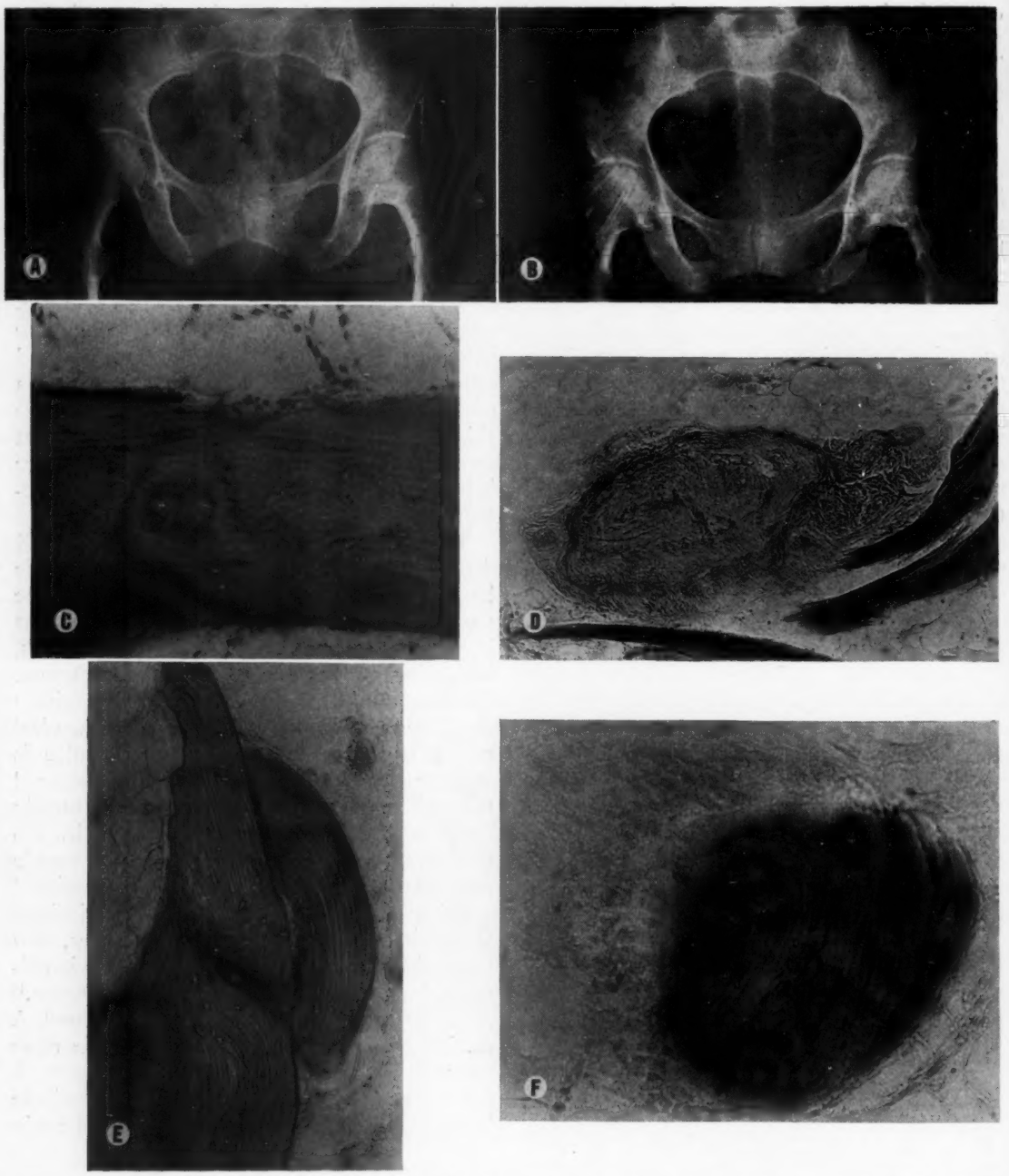


FIG. 2. Case II. (*A*) Fracture of left femoral neck eleven months after irradiation, five months after onset of symptoms. (*B*) Six months after insertion of frozen homogenous ("bank") rib bone grafts into the head and neck of both femurs. (*C*) Photomicrograph of trabeculum showing vascular absorption (430×). (*D*) Almost completely obliterated vessel (200×). (*E*) New bone formed on partially absorbed and possibly partially necrotic trabeculum (170×). (*F*) Numerous osteoblasts along a trabeculum near the fracture site.

shows small focal areas of necrosis. The ligamentum teres contains patent vessels.

*Comment.* In spite of a moderate degree of displacement of the femoral head in this patient, the head remained viable and showed a normal reparative response to the fracture. Early internal fixation of the head would probably have prevented dis-

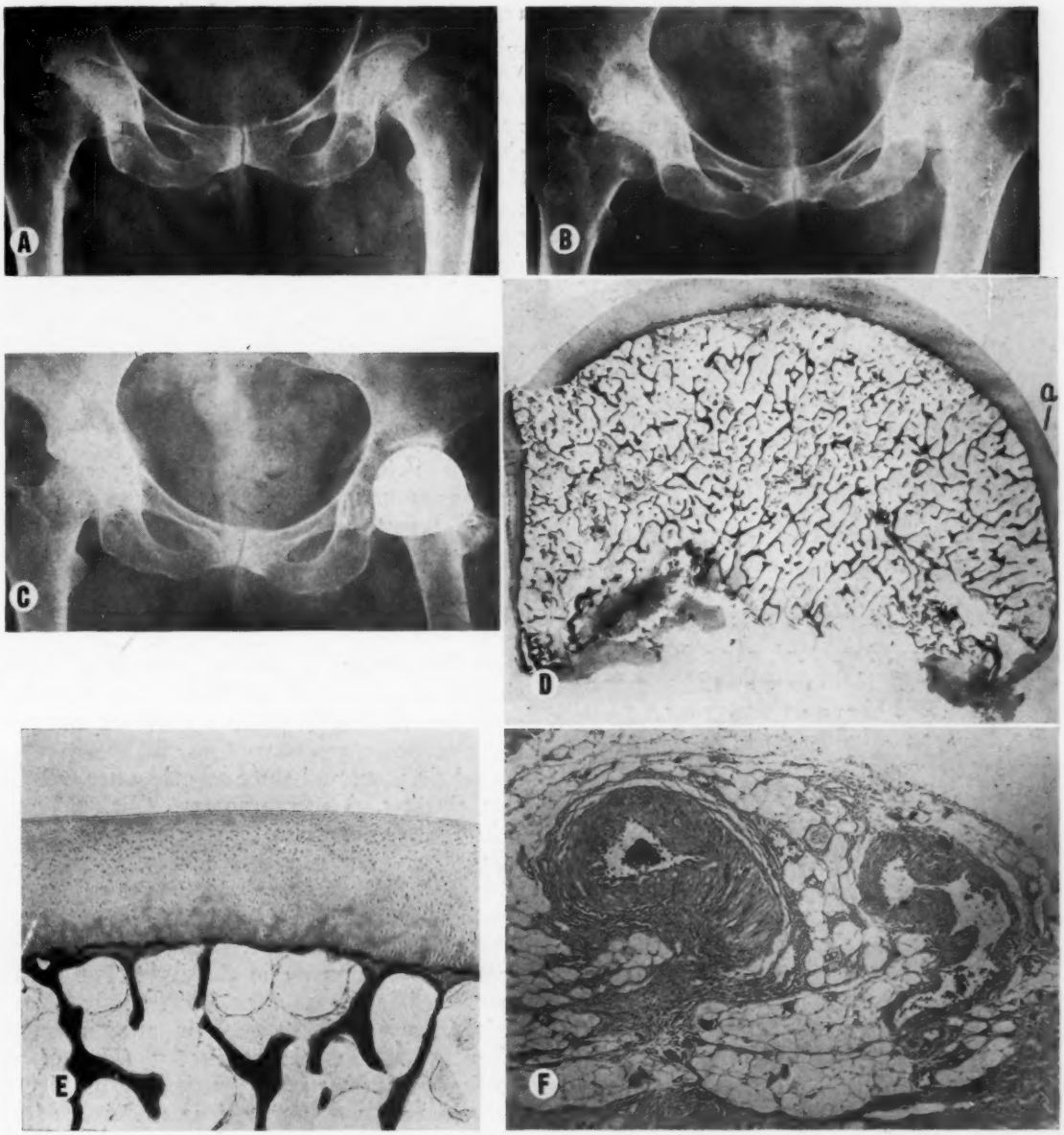


Fig. 3. Case III. (*A*) Roentgenogram eleven months following irradiation to the pelvis shows a slightly displaced subcapital fracture of the left femur. (*B*) Four months later there is further displacement of the fracture in spite of treatment by crutch walking. Note segmental right acetabular fracture and increased density. (*C*) Satisfactory vitallium mold arthroplasty nine months after operation. Acetabular fracture has healed. (*D*) Photomicrograph of a microscopic section of a slice of the head demonstrates viable atrophic bone (3×). (*E*) The cartilage appears normal. Subchondral cortex is thin (23×). (*F*) Subintimal thickening of an arteriole and vein (150×).

placement and resulted in bony union. Marked differences in the type of reparative response to the fracture are illustrated by the following 2 patients.

Case IV. F. L., a woman, aged seventy, was treated with 4,235 r parametrial dose and 5,090 r (air) transvaginally for a carcinoma of the cervix. Biopsy of the femoral head and neck and insertion of a rib bank bone graft was done twenty-five months after completion of radiation therapy, and four months after onset of

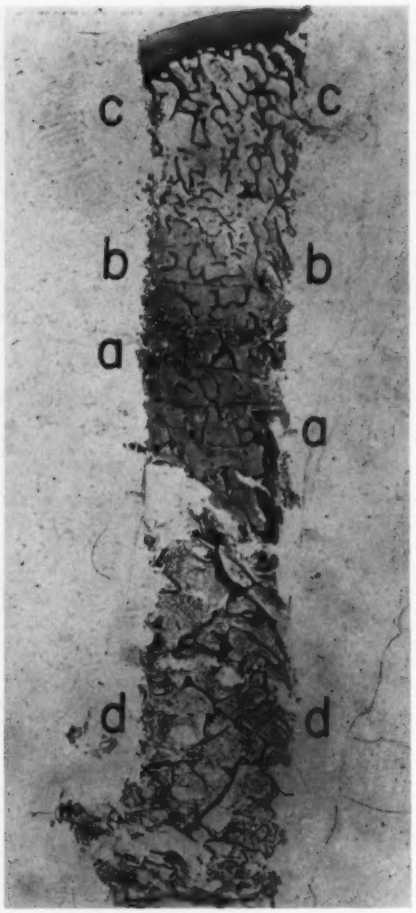


FIG. 4. Case IV. Photomicrograph of microscopic section of biopsy. Area *a-a:* Zone of fibrous tissue at the fracture site. Numerous spicules of dead bone in this area. Area *b-b:* Zone of osteoporotic viable trabeculae. Area *c-c:* Partial necrosis of trabeculae with new bone on old trabeculae. Area *d-d:* Normal hematopoietic marrow.

pain in the right hip. Microscopically (Fig. 4), the wide zone of fibrous tissue at the fracture line (*a*) contains numerous small fragments of broken trabeculae. There is much absorption of bone with only minimal new bone formation. The trabeculae just proximal (*b*) to the fracture line are thin but viable. In the subchondral region (*c*) there is partial necrosis of the old trabeculae with new bone along the margins and new haversian canals with living bone around them. The marrow consists of fat and fibrous tissue in the head and neck and hematopoietic elements in the intertrochanteric region (*d*).

CASE V. B. C., a woman, aged forty-six, was treated for a carcinoma of the cervix with 3,790 r parametrial dose and 5,000 r (air) transvaginally. Thirty-seven months later, after five months of prodromal pain in the thigh and hip, an undisplaced subcapital fracture (Fig. 5*A*) of the femoral neck was found. Biopsy taken at the time of treatment with a tibial crest bone transplant (Fig. 5*B*) disclosed considerable new bone formation in the zone about the fracture line (Fig. 5*C*). The findings were otherwise similar to those described above except that the degree of osteoporosis was not as marked in this patient of forty-six years. Union of the fracture occurred in three months (Fig. 5*B*).

CASE VI. R. W., at the age of fifty, received 5,200 r parametrial dose for a carcinoma of the cervix. Roentgenograms (Fig. 6*A*), made one year later at the time of a genitourinary tract examination, were normal. Two years after radiation therapy the patient was treated with crutches for pain in the left hip. Four years after irradiation, roentgenograms (Fig. 6*B*) show a healed fracture of the left femoral neck an increased density of the acetabular cortex. A spontaneous fracture of the right hip occurred six years and three months after radiation therapy. A roentgenogram (Fig. 6*C*) at this time demonstrates a subcapital fracture of the right femur with moderate varus displacement. The left acetabular area of increased density is surrounded by a radiolucent zone. There is a suggestion of a fracture through the acetabulum. Increase in density about both sacroiliac joints is apparent. The fracture of the right femoral neck remained ununited in spite of a subtrochanteric osteotomy (Fig. 6*D*). Twelve years after radiation therapy the right femoral head was removed at the time of a vitallium mold reconstruction operation. Microscopically, a section of the head (Fig. 6*E*) reveals extremely fragile trabeculae, fatty marrow, pseudarthrosis of the nonunion site and only a few areas of degenerated cartilage. These changes are similar to those described for old ununited fracture of the femoral neck with a viable head.[22]

Interesting, but apparently incidental, findings in this patient were sclerosis about the sacroiliac joints and the segmental acetabular irradiation damage. This latter change has been noted before in association with necrosis and collapse of the femoral head.[8]

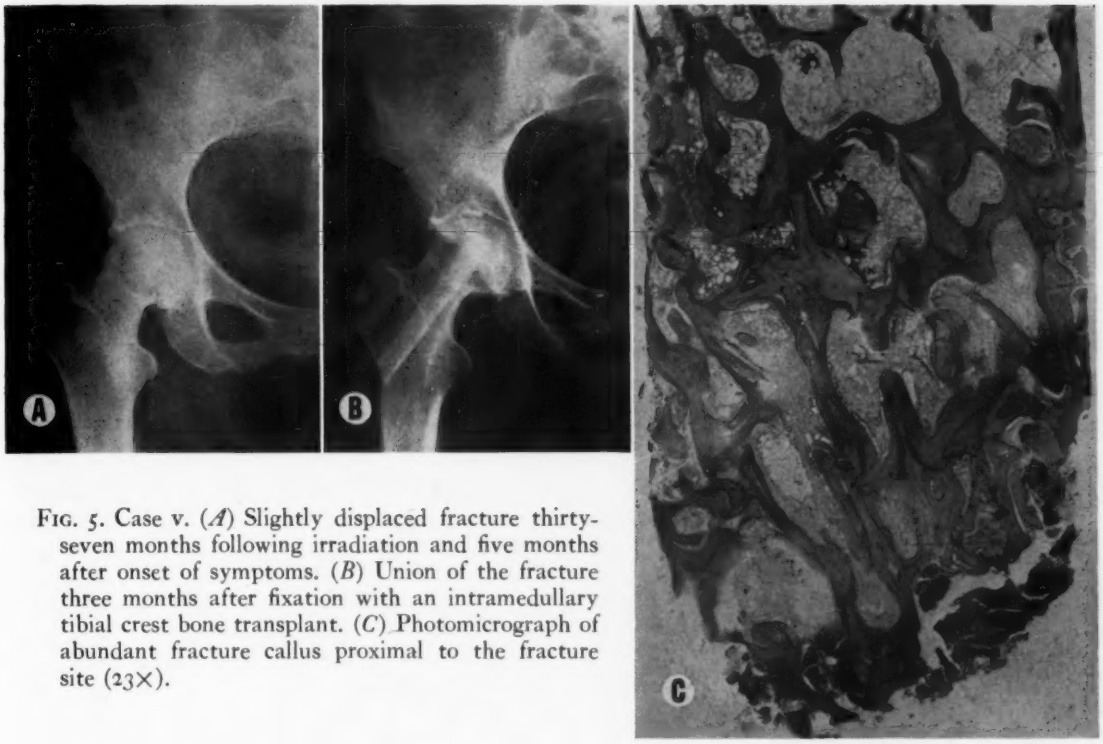


Fig. 5. Case v. (*A*) Slightly displaced fracture thirty-seven months following irradiation and five months after onset of symptoms. (*B*) Union of the fracture three months after fixation with an intramedullary tibial crest bone transplant. (*C*) Photomicrograph of abundant fracture callus proximal to the fracture site (23×).

In the following patient, a segmental acetabular fracture was complicated by trauma with the result that separation of the necrotic fragment and necrosis and breakdown of the femoral head occurred.

Case vii. E. O., a woman, aged forty-eight, voluntarily left the hospital in March, 1948, after receiving a tumor dose of only 1,458 r to the parametrium for a carcinoma of the cervix, She then received two intermittent courses of irradiation elsewhere over the next eleven months of 3,550 r (air) and 4,400 r (air). A roentgenogram made in February, 1949 (Fig. 7*A*) at the time of completion of the second course shows increased density of the weight-bearing portion of the acetabulum with a zone of reduced density above.

Two months later, April, 1949, the patient fell with her full weight on her right knee. She developed pain in her right hip and limp on walking. Roentgenograms (Fig. 7, *B* and *C*) four months apart reveal a segmental acetabular fracture with moderate increase in density of the fragment. This was thought to be metastatic so an additional course of 3,000 r (air) to the right pelvis was given. Fragmentation of the superior lateral portion of the head and the acetabular segment is seen in roentgenograms (Fig. 7*D*) made nineteen months (August, 1950) after the injury and onset of pain in the hip. At operation, a thickened capsule, considerable granulation tissue, and necrotic bits of bone and cartilage were encountered. On preparing the head for a vitallium mold, free bleeding from all areas was noted. A section (Fig. 7*E*) of the fragmented head demonstrates necrotic articular cartilage and subchondral cortex with new bone along the margins, and fibrous marrow containing necrotic bits of bone. Creeping substitution about a haversian canal lined by osteoblasts is shown in a high power photomicrograph of necrotic acetabular bone (Fig. 7*F*).

*Comment.* It is obvious that this patient does not illustrate the usual type of irradiation change in the bony pelvis. Two factors must be considered. Direct mechanical trauma to the hip joint and probably additional irradiation to the area which produced more severe damage to the bone than one ordinarily sees after irradiation for a pelvic malignancy.

Pathological changes similar to those

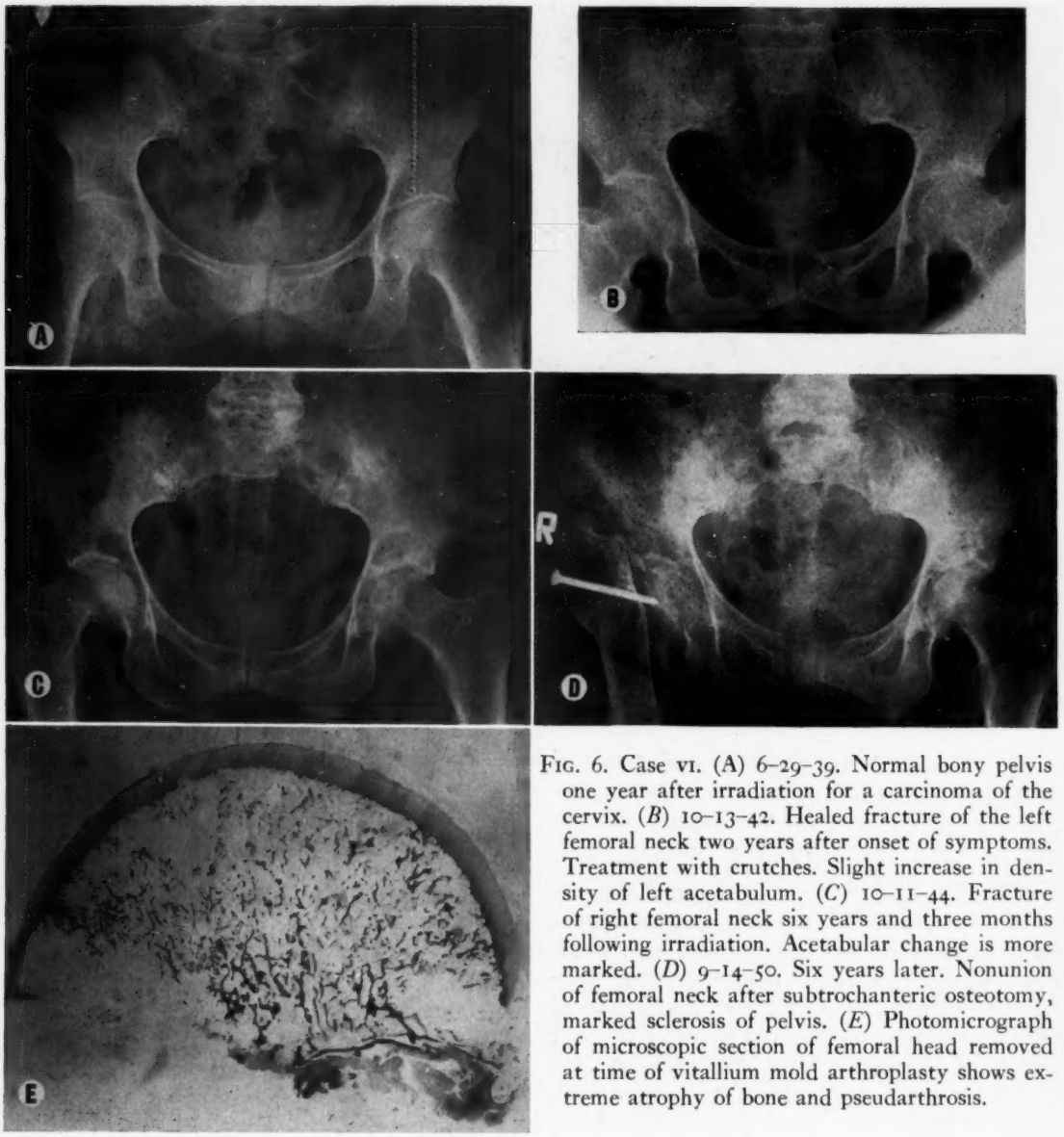


FIG. 6. Case VI. (A) 6–29–39. Normal bony pelvis one year after irradiation for a carcinoma of the cervix. (*B*) 10–13–42. Healed fracture of the left femoral neck two years after onset of symptoms. Treatment with crutches. Slight increase in density of left acetabulum. (*C*) 10–11–44. Fracture of right femoral neck six years and three months following irradiation. Acetabular change is more marked. (*D*) 9–14–50. Six years later. Nonunion of femoral neck after subtrochanteric osteotomy, marked sclerosis of pelvis. (*E*) Photomicrograph of microscopic section of femoral head removed at time of vitallium mold arthroplasty shows extreme atrophy of bone and pseudarthrosis.

described in Case 1 were noted in 2 other patients whose fractures were treated by intramedullary bone transplants.

## DISCUSSION

It is apparent from the pathologic material studied that in the usual patient with an irradiation fracture of the femoral neck the dose of radiation received by the hip joint is below that producing complete devitalization. Slaughter[23] estimates the average dose to the head and neck at 3,000 r. The tolerance dose of the femoral head and neck has been estimated at 3,840–4,320 r.[9] That amount of radiation is said to produce temporary to prolonged inactivation of bone regeneration.[27] Aseptic necrosis of the head as seen in about one-third of traumatic fractures of the femoral neck is actually a rare occurrence following spontaneous irradiation fracture. It has not been noted in 25 of our patients with thirty-two fractures. The subcapital zone of osteoporosis produced by the irradiation

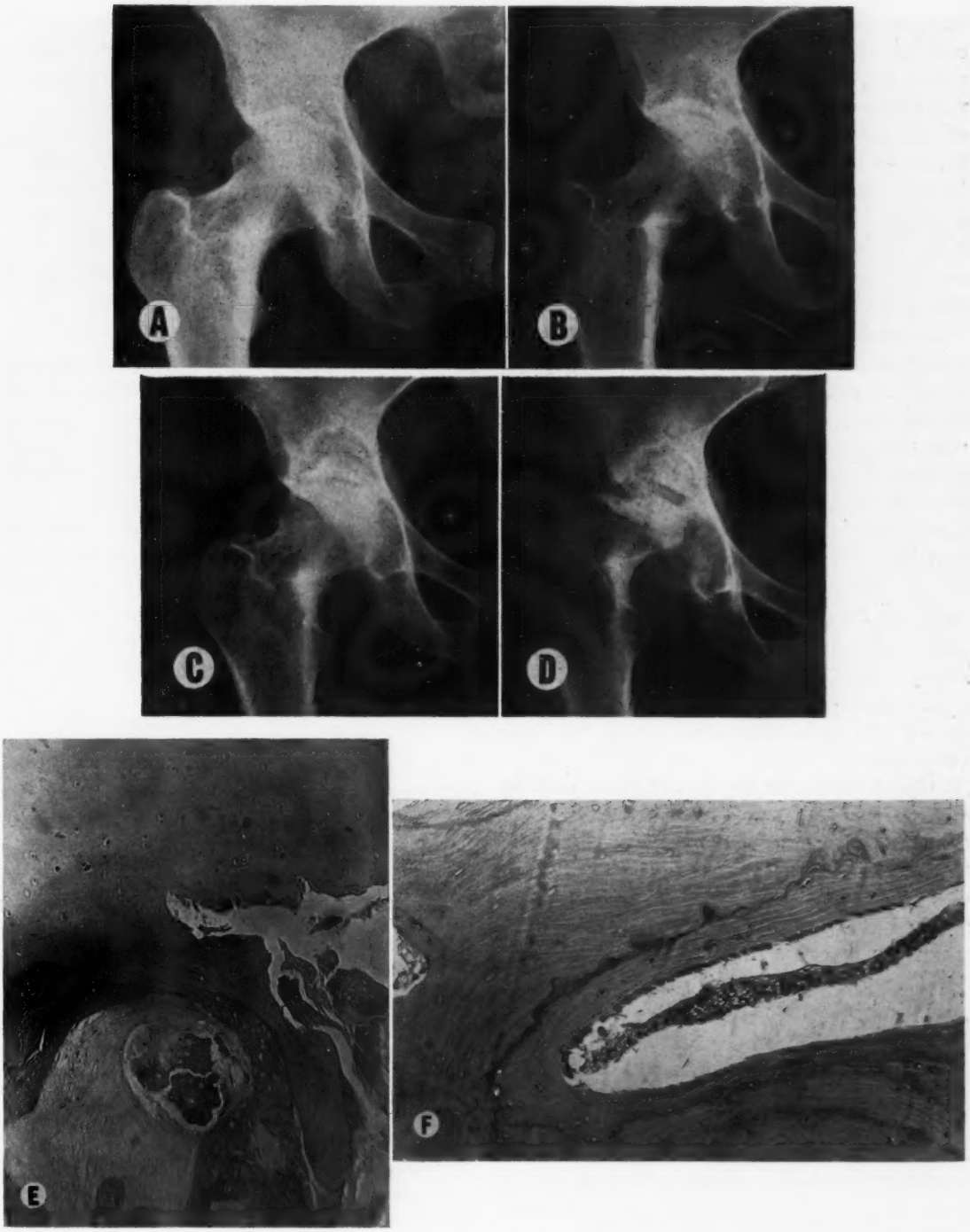


Fig. 7. Case VII. (*A*) 2–9–49, At time of completion of third course of pelvic irradiation. There is an increased density in the neck inferiorly. (*B*) 5–25–49. One month after injury to the right hip. Early acetabular changes. (*C*) 9–29–49. Four months later, a segmental acetabular fracture is present. (*D*) 8–28–50. One year later, fragmentation of femoral head and acetabulum. (*E*) Photomicrograph of necrotic articular cartilage and cortex. New bone along dead bone. Small spicules of necrotic bone within fibrous marrow. (90×). (*F*) Creeping substitution of necrotic acetabular bone. Osteoblasts line a vascular channel (170×).

renders the neck of the femur more susceptible to a "stress" or "insufficiency" type of fracture. This gives rise to symptoms many months before roentgen proof of the fracture. Interruption of the circulation to the head and subsequent necrosis is therefore unlikely. In general, vascular damage by the irradiation was not sufficient to impair the healing and repair response noted in these fractures. The absorptive changes are on a vascular basis.

Osteoclastic activity seems to play a minimal role in producing osteoporosis noted in these patients. The presence of osteoblasts, on the other hand, was not uncommon where new bone was being formed (Fig. 2*F*). True increase in density of some trabeculae, as seen on the roentgenogram, is explained by the formation of new bone on old trabeculae. This may lead to an erroneous roentgenographic diagnosis of aseptic necrosis of the head because of relative density differences between the head and neck.

The partial necrosis of the subchondral cortex and trabeculae away from the fracture site is probably secondary to irradiation damage to osteocytes directly and to a lesser degree as a result of irradiation injury to the blood supply. That focal areas of necrosis are not necessarily due to the fracture is evident by the presence of this finding in a biopsy obtained where no fracture had yet occurred (Case 11). The relatively normal healing response described should lead to a satisfactory union of the fracture, providing the same surgical principles are applied early that pertain to other fractures of the hip joint. An analysis of the results of treatment of irradiation fracture of femoral neck will be the subject of a subsequent paper.

## SUMMARY AND CONCLUSIONS

1. Pathologic material from patients with irradiation damage to the hip joint was studied. These patients received intensive irradiation for pelvic malignancy.

2. The most important of the pathologic changes observed is osteoporosis. Osteoclastic activity in the osteoporotic bone is absent. A "stress" type subcapital fracture occurs through an osteoporotic zone.

3. Adequate callus occurs at the fracture, indicating a good repair response.

4. Secondary findings indicative of general injury and repair changes are new bone about old, partially necrotic or atrophic trabeculae, occasional thickening of vessel walls, and marrow fibrosis.

5. Segmental acetabular irradiation fracture subjected to additional trauma resulted in necrosis and separation of the area and fragmentation of the femoral neck. In three other patients with this complication, healing occurred spontaneously.

6. The changes which have been described are sufficient to make patients irradiated for pelvic malignancy more susceptible to fracture of the femoral neck; however, early treatment of the fracture is usually satisfactory. The gynecologist and radiologist are in the most favorable position to recognize these fractures.

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## DISCUSSION

DR. PAUL C. HODGES, Chicago, Ill. Dr. Bonfiglio has shown us that in something less than 2 per cent of the women who receive irradiation for pelvic neoplasm there is injury to one or both of the hip joints, and that incidence arises as the survival rate becomes longer. The trouble usually comes late, twenty-four or thirty-six months or longer after irradiation, but has been seen in less than six months.

Most of the patients are old but their bones histopathologically show osteoporosis even greater than age alone would account for. It is almost as though irradiation had abnormally aged the bone. But a few of the women are young and suffer fracture without any prodromal osteoporosis. The lesions are clear enough. Of course, one should do everything that he can do to reduce the amount of radiation that reaches normal bone but when he does his very best, he must then be philosophical and accept this complication as a price that is not too great to pay for the benefits that are obtained.

Another lesson is that when fractures do occur, they should be treated promptly and vigorously, and that if this is done, repair will occur just as it does in straightforward traumatic fractures.

DR. LENT C. JOHNSON, Washington, D. C. In the 100 or so cases that have been found in the literature has comparable irradiation in the male pelvis ever produced the same lesion in males?

DR. BONFIGLIO (closing). In answer to Dr. Johnson's question, yes, it has been noted in about 3 reported cases and the findings were said to be the same in those instances.

I wish to thank Dr. Hodges for his kind remarks and discussion.

# ROENTGEN THERAPY THROUGH A GRID FOR ADVANCED CARCINOMA*

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THE Coutard method of divided doses was a significant advance in deep roentgen therapy. With this technique radiation results were immeasurably improved. The use of supervoltage roentgen therapy and the various modifications of the Coutard technique represent the important advances in radiation therapy in the past twenty years. Supervoltage roentgen therapy at the present time is limited to large cancer centers. It would be of great advantage to patients with deeply seated cancers amenable to roentgen treatment, if the tumor doses obtainable with supervoltage equipment could be approximated with 200 to 400 kv. machines. The revival by Hirsch Marks[17] of the almost forgotten method of increasing tumor dosage by giving greater skin doses through a lead grid is a step in this direction.

The principle of irradiating through multiple small areas instead of one large portal, as is now commonly done, is not new. It was first described by Alban Köhler in 1909,[14] rediscovered by F. Liberson in 1933,[15] and more recently utilized in a modified form by Goldfeder,[3,4] Grynkraut[5] and Jolles.[12] The proponents of this method state that if many small areas are exposed to irradiation larger doses will be tolerated by the skin than when single large portals are utilized.

Early in 1950, after reviewing Marks' material, we decided to investigate this method of irradiation on patients with advanced malignant disease. It is the intent of this report to relate our results. We shall describe the more important features of such irradiation so that those interested may benefit from our experiences.

## MATERIAL

The material consists of 35 patients, most of whom were treated at the Montefiore Hospital. Several cases from the private practice of one of the authors (J.R.F.) are included. Many of the patients were irradiated recently; therefore, the follow-ups are of short duration.

All of the patients had far advanced disease so that little could be expected with conventional radiotherapy. They were also poor candidates for grid therapy, therefore therapeutic results will not be stressed. The cases will be discussed according to the anatomical site of the primary lesion.

Eleven patients can be classified under head and neck, 9 under chest, 8 of whom had bronchogenic carcinoma and 1 a postoperative recurrence of a mediastinal teratoma. There were 6 in the gynecologic group, 4 of whom had ovarian cancer and 2 had cancer of the uterine cervix; 4 in the gastrointestinal group, including 2 cases of carcinoma of the stomach; 1 of the esophagus and 1 a recurrence of a postoperative carcinoma of the rectum. Three patients were treated for carcinoma of the bladder. One patient had Hodgkin's disease and 1 had metastatic supraclavicular nodes from carcinoma of the breast.

This material is tabulated in Table 1, giving diagnosis, duration and number of treatments, fields treated, total air dose, tumor depth, skin and tumor doses for both open and closed areas. The results of treatment are listed in the last column.

## TECHNIQUE

Two hundred kilovolt and 400 kv. roentgen rays were used. Most of the patients reported

* Presented at the Fifty-second Annual Meeting, American Roentgen Ray Society, Washington, D. C., Sept. 25–28, 1951.
† Fellow of the American Cancer Society.

## TABLE I

DIAGNOSIS, TECHNIQUE, DOSAGE AND RESULTS OF CASES TREATED

| Case No. | Patient | Age | Sex | Hosp. No. | Diagnosis | Duration | No. of Treatments | Field | Total Air Dose in Roentgens | $r_0$ Skin Dose Open | $r_0$ Skin Dose Closed | Tumor Depth | $r_d$ Tumor Dose Open | $r_d$ Tumor Dose Closed | Results |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | cm. | | | | cm. | | | |
| 1 | G.F. | 35 | M | 52379 | Lymphoepithelioma nasopharynx | 19 days | 15 | Rt. lat. 8×10 | *15,000 | 15,600 | 2,700 | 6 | 6,975 | 3,150 | Palliation—short duration |
| | | | | | | | 11 | Rt. orbit and antrum 6×8 | 12,900 | 14,450 | 2,130 | 6 | 5,620 | 2,130 | |
| 2 | N.S. | 74 | M | 53630 | Cancer left buccal mucosa | 4 wk. | 19 | Left lat. jaw 8×8 | 21,100 | 23,600 | 3,680 | 4 | 13,250 | 4,520 | Lesion disappeared; irradiation necrosis |
| 3 | P.W. | 82 | M | 19053 | Cancer soft palate | 4 wk. | 21 | Rt. lat. 10×12 | 19,000 | 21,500 | 3,160 | 6 | 9,200 | 4,100 | Primary uncontrolled |
| 4 | J.V. | 75 | M | 52238 | Cancer soft palate, rt. tonsil, cheek | 3½ wk. | 17 | Rt. lat. 10×12 | 20,200 | 22,800 | 4,050 | 4 | 13,300 | 4,850 | Lesion disappeared; patient died |
| 5 | G.J. | 70 | M | 53530 | Cancer left tonsil | 2½ wk. | 12 | Rt. lat. 8×10 | 14,400 | 16,300 | 2,520 | 9 | 3,900 | 1,820 | Palliation; lesion persists |
| 6 | B.S. | 71 | F | Pvt JRF | Cancer of tongue, floor of mouth | 4 wk. | 22 | Rt. lat. jaw 8×10 | 14,500 | 16,380 | 2,540 | 4 | 9,000 | 3,060 | Lesion persisted; patient died |
| | | | | | | 2 wk. | 9 | Rt. lat. jaw 8×6 | 7,500 | 8,400 | 1,240 | 6 | 3,260 | 1,240 | |
| 7 | W.I. | 50 | M | Pvt JRF | Cancer nasopharynx | 2 wk. | 11 | Rt. lat. 14Ø | 11,000 | 12,650 | 2,360 | 7 | 4,800 | 2,440 | Lesion diesappeared; short duration |
| 8 | M.C. | 45 | M | 55265 | Cancer larynx with extension | 2½ wk. | 7 | Rt. lat. neck 12×10 | 8,400 | 9,560 | 1,680 | 4 | 5,500 | 2,030 | Palliation; short duration |
| | | | | | | | 7 | Left lat. neck 12×10 | 8,400 | 9,560 | 1,680 | 4 | 5,550 | 2,030 | |
| 9 | G.L. | 65 | F | 46046 | Cancer larynx left subglottic | 3½ wk. | 14 | Rt. lat. neck 12×10 | 15,400 | 17,500 | 3,080 | 4 | 10,100 | 3,700 | Lesion persisted; patient died |
| 10 | A.S. | 51 | F | 53370 | Cancer right antrum | 4 wk. | 22 | Rt. lat. 8×10 | 23,950 | 27,000 | 4,180 | 6 | 10,750 | 4,430 | Palliation; short duration |
| 11 | N.M. | 67 | M | 52659 | Postop. cancer larynx, left cervical nodes, metastases | 4 wk. | 20 | Left lat. 10×10 | 24,000 | 27,150 | 4,450 | 4 | 15,350 | 5,450 | Palliation; short duration |
| 12 | L.B. | 50 | M | 52361 | Cancer rt. main bronchus | 4 wk. | 17 | Post. chest 12×15 | 20,400 | 23,600 | 4,530 | 12 | 3,780 | 2,550 | Palliation; short duration |
| | | | | | | 2 wk. | 9 | Ant. chest 12×15 | 10,800 | 12,500 | 2,400 | 15 | 1,295 | 910 | |
| 13 | A.O. | 76 | M | 51182 | Cancer left main bronchus | 4 wk. | 20 | Ant. chest 10×10 | 24,000 | 27,100 | 4,450 | 10 | 5,570 | 3,000 | Palliation; short duration |
| 14 | R.K. | 55 | M | 52687 | Cancer bronchus RUL | 3½ wk. | 18 | Ant. chest 15×15 | 16,800 | 19,750 | 3,880 | 10 | 4,720 | 2,960 | Palliation; short duration |
| | | | | | | 3 wk. | 14 | Post. chest 15×15 | 16,800 | 19,750 | 3,880 | 15 | 2,150 | 1,530 | |
| | | | | | | 3 wk. | 14 | Rt. supraclavic. 6×8 | 16,800 | 18,800 | 2,770 | 4 | 10,090 | 3,280 | |
| 15 | D.N. | 71 | M | 50449 | Cancer LML, post. | 4 wk. | 18 | Post. chest 15×15 | 21,600 | 26,700 | 4,970 | 9 | 7,150 | 4,300 | Palliation; short duration |
| | | | | | | 3 wk. | 16 | Left lat. 10×15 | 19,200 | 22,100 | 4,130 | 12 | 3,460 | 2,310 | Palliation; short duration |
| 16 | W.S. | 59 | M | 52237 | Cancer LUL bronchus | 3½ wk. | 10 | Ant. chest 15×15 | 11,800 | 13,900 | 2,720 | 9 | 3,980 | 2,360 | Palliation; short duration |
| | | | | | | | 10 | Post. chest 15×15 | 11,800 | 13,900 | 2,720 | 12 | 2,350 | 1,590 | |
| 17 | M.T. | 63 | M | 52853 | Cancer LML bronchus | 3 wk. | 14 | Ant. chest 12×15 | 16,800 | 19,350 | 3,730 | 15 | 2,030 | 1,410 | Palliation; short duration |
| | | | | | | 4 wk. | 20 | Post. chest 13×15 | 24,000 | 27,800 | 5,520 | 15 | 3,000 | 3,110 | |
| 18 | M.M. | 60 | M | 45556 | Cancer RUL bronchus | 3 wk. | 13 | Ant. chest 10×12 | 15,600 | 17,800 | 3,120 | 12 | 2,540 | 1,580 | Palliation; short duration |
| | | | | | | 3 wk. | 12 | Post. chest 10×12 | 14,400 | 16,400 | 2,880 | 12 | 2,350 | 1,450 | |
| 19 | R.A. | 48 | M | Pvt JRF | Cancer LLL bronchus | 4½ wk. | 19 | Ant. chest 12×15 | 13,400 | 15,450 | 2,980 | 10 | 3,600 | 2,180 | Palliation; short duration |
| | | | | | | 2½ wk. | 12 | Post. chest 12×15 | 10,700 | 12,300 | 2,380 | 11 | 2,390 | 1,520 | |
| 20 | K.H. | 60 | F | Pvt JRF | Teratoma mediastinum metastases left lung | 3 wk. | 16 | Ant. chest 9×9 | 13,200 | 14,850 | 2,310 | 9 | 3,500 | 1,050 | Metastases disappeared; short duration |
| 21 | E.P. | 45 | F | 51498 | Cystadenocarcinoma ovary | 4 wk. | 17 | Ant. pelvis 15×20 | 16,400 | 20,200 | 3,820 | 10 | 4,800 | 3,165 | No improvement; patient died |
| 22 | F.N. | 47 | F | 52811 | Adenocarcinoma ovary | 2 wk. | 13 | Ant. pelvis 15×18 | 12,900 | 15,700 | 3,000 | 8 | 5,050 | 2,800 | Transient palliation; patient died |
| 23 | M.B. | 66 | F | 51250 | Cancer ovary | 3 wk. | 17 | Ant. pelvis 10×20 | 20,400 | 23,600 | 4,700 | 9 | 6,740 | 3,940 | Palliation; short duration |
| 24 | H.F. | 35 | F | Pvt JRF | Cancer ovary | 4 wk. | 17 | Ant. LLQ 10×15 | 15,700 | 18,050 | 3,380 | 8 | 5,860 | 3,140 | No improvement; patient died |
| 25 | B.L. | 59 | F | 52467 | Cancer cervix (Stage IV) | 5 days | 5 | Ant. pelvis 14×17 | 5,400 | 6,450 | 1,250 | 6 | 2,940 | 1,480 | Treatment interrupted by peritonitis |
| 26 | E.J. | 42 | F | 49975 | Cancer cervix (Stage IV) | 4 wk. | 17 | Ant. pelvis 15×20 | 16,200 | 20,000 | 3,780 | 10 | 4,750 | 3,130 | No improvement; patient died |
| 27 | R.S. | 52 | M | 51919 | Cancer bladder | 4 wk. | 20 | Ant. suprapubic 10×10 | 23,400 | 26,400 | 4,330 | 6 | 11,100 | 4,800 | Some improvement; patient died |
| 28 | J.J. | 47 | M | 45628 | Cancer bladder | 4 wk. | 21 | Ant. suprapubic 10×10 | *20,500 | 21,350 | 3,900 | 6 | 9,550 | 4,830 | Improvement; radiation necrosis |
| 29 | H.Z. | 65 | M | Pvt JRF | Cancer bladder | 4 wk. | 20 | Ant. suprapubic 10×12 | 23,400 | 26,700 | 4,680 | 5 | 13,200 | 5,530 | Primary disappeared; 1 year post treatment |
| 30 | E.W. | 71 | M | 53665 | Cancer stomach | 4 wk. | 21 | Left post. 15×15 | *20,500 | 21,750 | 4,650 | 10 | 6,260 | 4,300 | No improvement; patient died |
| 31 | P.C. | 44 | M | 53592 | Cancer stomach | 3 wk. | 16 | Ant. abdomen 15×15 | *15,500 | 16,400 | 3,500 | 10 | 4,720 | 3,240 | No improvement; patient living |
| | | | | | | 1½ wk. | 9 | Post. abdomen 15×15 | *9,000 | 9,550 | 2,040 | 15 | 1,530 | 1,040 | |
| 32 | R.S. | 73 | F | 51282 | Cancer esophagus | 5 wk. | 23 | Ant. mediastinum 7×13 | 21,400 | 24,200 | 3,960 | 12 | 3,300 | 2,030 | No improvement; patient died |
| 33 | A.W. | 50 | M | Pvt JRF | Recurrent cancer rectum | 3 wk. | 15 | Ant. pelvis 10×15 | 16,100 | 18,500 | 3,542 | 8 | 6,120 | 3,220 | No improvement; patient died |
| 34 | M.B. | 46 | F | 51466 | Met. lt. supraclavic. nodes (cancer breast) | 2½ wk. | 13 | Left supra and infraclavic. 12×12 | 15,600 | 17,950 | 3,360 | 4 | 10,450 | 4,030 | Lesion disappeared; 14 months post treatment |
| 35 | M.M. | 54 | M | 49158 | Hodgkin's disease | 4 wk. | 18 | Ant. LLQ 20×15 | 16,200 | 19,950 | 3,780 | 10 | 4,750 | 3,130 | Lesion disappeared; radiation necrosis |

* Treated with 400 kv. machine.

FIG. 1. Photograph of cone with a movable grid as used on a patient.

in this paper were treated with the 200 kv. machine. Four patients (identified by an asterisk in Table 1) were treated with the 400 kv. machine.

*200 kv. Roentgen Rays.* The 200 kv. roentgen rays, half-value layer 0.94 mm. Cu. were used at a target skin distance of 50 cm. The grids were made of lead rubber 4 mm. thick with a lead equivalent of 1.3 mm., which transmitted less than 1 per cent of the incident roentgen-ray beam. The diameter of the holes was 1 cm. and the distance between centers was 1.4 cm., giving a grid with a 40 per cent open area and a 60 per cent covered area. These grids were made with a template constructed in our machine shop. Such a template insures uniformity of holes and spacings.

Care should be taken to expose the same area of skin each time the grid is applied. This was accomplished by marking the skin under a number of openings with a dye such as carbolfuchsin or gentian violet and carefully aligning the grid with these marks.

*400 kv. Roentgen Rays.* When the 400 kv. roentgen rays, half-value layer 3.3 mm. Cu, target skin distance 60 cm. were used, the technique was slightly different. In order to reduce the transmitted radiation, the grid was made of 5 mm. of lead and 2 mm. aluminum (1 mm. would also be adequate) instead of lead rubber. This grid transmitted 1.6 per cent of the incident roentgen ray beam through the closed areas. The spacings were the same as for the lead rubber grids.

Where possible, the grid was placed directly on the skin. In other cases, especially for curved surfaces, the grid was inserted in a cone specially designed by one of the authors (L.E.J.)[8] to permit the grid to be easily moved in any direction in a plane parallel to the base of the cone, thus allowing precise positioning.

This cone is only useful where there is a light localizer for showing the outline of the field and spots (Fig. 1). The roentgen tube was aligned so the rays emerged vertically. The patient was positioned with the portal parallel to the base of the cone. The cone was brought down to the field and the diaphragm set to give the outlined field on the skin. The tube was raised just sufficiently to permit marking of the light spots with the grid inserted. This cone skin distance was recorded. With the diaphragm set and the grid removed, the field and cross lines as outlined by the light localizer at this distance were marked on the patient's skin. The grid was re-inserted and the cone brought down to the portal, ready for treatment.

Each time the patient was positioned for treatment, the cone was placed at the same distance from the patient, the diaphragm opened to give the outlined field, the cross lines of the light localizer matched and the grid inserted into the cone and moved so that the circles of light were over the previously marked spots. The cone was then brought down to the field and treatment given.

*Dosage.* Treatment was generally started with a dose of 600 to 800 roentgens in air. If no undue radiation reaction was encountered, the dosage was increased up to 1,200 r daily. Cases with marked respiratory difficulty due either to massive involvement in the larynx or the mediastinum were treated with doses of 300 r to 600 r in air per treatment until the respiratory symptoms improved, when the radiation was gradually increased to a maximum of 1,200 r in air daily. The maximal total air dose, when a single portal was used, was 24,000 r. Many individuals were treated over two portals and, in these instances, the total dose per portal varied from 12,000 to 16,000 r in air. The greater dose was administered to the portal closer to the tumor. At the beginning of this investigation, an arbitrary dose of 24,000 r in air was given to a single portal overlying the growth as advocated by Marks.

As depth doses became available,[9] our objective was the delivery of a predetermined tumor dose of 5,000 to 8,000 $r_d$ under the openings. Naturally, this objective was not possible for all patients. The treatment was administered usually over a period of four to six weeks, de-

pending on whether one or more portals were utilized. The irradiation period was rarely greater than four weeks for any single portal.

### PHYSICS

When the work with grid therapy was initiated, it became apparent that depth dose data were a necessity. After this investigation was begun, Loevinger and Minowitz[16] published their findings.

Depth dose measurements were made in a masonite presdwood phantom. The method has been described in a previous publication.[9] The dosage rates were measured under the central opening and under the central covered portion for various depths and field sizes. Another set of measurements were made to obtain the *average* dose at any depth.

With grid therapy there is no single depth dose for a given depth. The depth dose consists of two distinct parts, both at the surface and in the underlying tissues. One portion receives the direct radiation through the opening plus the secondary radiation produced in the volume of tissue, the other portion receives only the secondary radiation plus the small amount transmitted through the protective lead rubber or lead, about 1–1.5 per cent in our case. When an average of these two is made, one must keep clearly in mind that there is really no physical average but only a calculated one. The portions underneath the holes receive more at all levels than the portions underneath the closures. The difference decreases as the depth increases for two reasons: (1) the greater the depth, the larger is the fraction due to secondaries; (2) even if the positioning of the grid at the surface is the same, because the angling of the tube at each setting may be slightly different, the radiation coming through a hole may strike a portion of the tissue previously in the shadow of the protective material. Thus at a depth the dose tends to become more homogeneous.

Figure 2 (Case 10) shows that the field is nonuniform at a depth. A distinct grid pattern is visible on the buccal mucosa at a depth of 5 cm. after treatment of the lateral face for a carcinoma of the antrum.

Table II lists the depth doses obtained with the grid under the open areas, closed areas and the weighted averages for the 200 kv. radiation.

The depth doses for 400 kv. and those at the edge of the field with both 200 and 400 kv. will be published at a future date.[19]

Fig. 2. Grid pattern on buccal mucosa.

It is of interest to compare the dose received at the skin and various depths in grid therapy with that received in conventional therapy using the same factors. Table III is a comparison of the number of roentgens delivered with the grid if skin tolerance is given, with that received without the grid for a 10 by 15 cm. field, 200 kv., 50 cm. target skin distance, half-value layer 1 mm. Cu, when treatment is given over a month.

Table IV lists similarly the comparative depth doses for 400 kv. and a half-value layer of 3.3 mm. Cu at 60 cm. target skin distance.

The dose delivered to the tumor can be increased with grid therapy for two reasons: (1) because the skin tolerance is greater with the grid than without it and massive doses can be given, (2) under the covered portion the tumor dose increases over the skin dose up to a depth of from 6 to 9 cm., depending on the size of the area treated.

In Table V 200 kv. roentgen rays under the covered portion are compared with 2 mv. roentgen rays[18] and 22 mev. roentgen rays[10] for approximately equal areas treated. The super-

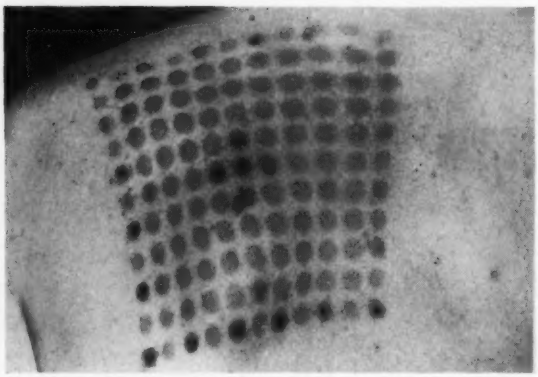

FIG. 3. Skin reaction showing grid pattern ten days after treatment began.

voltages were measured at 100 cm. target skin distance and the 200 kv. at 50 cm. target skin distance, the distances used in our therapy. The dose at 0.5 cm. depth is taken as 100 per cent. It will be noted that the depth dose under the closed part of the grid increases to 116 per cent. at a 3 cm. depth, and at a depth of 7 cm. the tumor dose is the same as the skin dose. With 22 mev. roentgen rays the dose is a maximum, 186 per cent, at a depth of 3 cm., and at 7 cm. is 163 per cent. With 2 mv. roentgen rays the dose at 7 cm. depth is 66 per cent. For both the radiations under the closures and that in the 20 mev. range, there is an increase in depth dose as the depth increases, then a leveling off followed by a decrease. In this manner grid irradiation simulates supervoltage irradiation in the 20 mev. range.

## REACTIONS

The reactions encountered are general and local.

*General.* In most cases there was exaggeration of pre-existing weakness. Of 10 patients treated over the abdomen, nausea, vomiting and diarrhea were observed in 4 where large portals were used. When the portals were small, the reactions were similar to those following conventional therapy. In the chest cases, no undue reactions were observed. For the head and neck group anorexia was severe.

*Local.* Skin: The skin reaction is similar in most respects to that observed with conventional roentgen therapy. Coutard described epidermitis (wet desquamation of skin) as occurring in twenty-six to twenty-eight days with dosages of 4,500 $r_0$, skin dose. With irradiation given through a grid, erythema, which conforms to the pattern of the open spaces in the grid, develops usually in four or five days when a dose of approximately 5,000 r in air has been delivered. However, a mild erythema has been observed within twenty-four hours with a dose of 600 r in air. In other cases, this reaction has been delayed up to 16 days with a dosage of 11,000 r in air (Fig. 3). As the treatment progresses, the erythema under the open portions of the grid becomes more pronounced and in three to four weeks usually extends to the covered areas, principally in the central portion of the treated field, as in Figure 4. The height of the reaction is reached in thirty to forty-five days with vesiculation and a moist desquamation of the exposed areas (Fig. 5). Healing is usually complete in fifty to eighty days. Subsequently, the areas under the openings show depigmentation and the covered regions tanning, given the appearance of a reversal of the grid pattern (Fig. 6). Some cases were followed for more than a year and now show atrophy of the irradiated skin, but nevertheless the skin remains soft and supple. Only 1 patient (Case 35) who was treated over the lower pelvis with a large portal, showed atrophy of the skin and marked thickening of the subcutaenous tissues three months following irradiation.

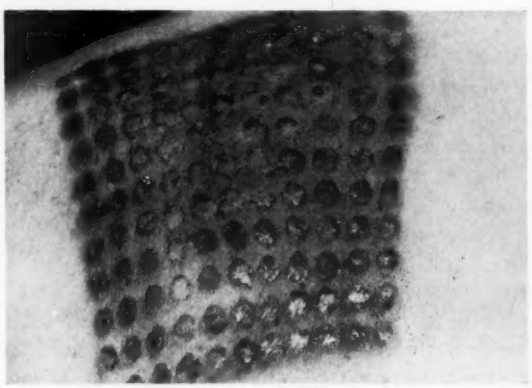

FIG. 4. Skin reaction which has extended to the covered areas, principally in the central portion of the field. Vesiculation under the open areas.

TABLE II

TABLE OF DEPTH DOSES WITH GRID FOR 100 ROENTGENS MEASURED IN AIR FOR DIFFERENT SIZES OF FIELDS

Target Skin Distance, 50 cm.; Half-Value Layer 0.94 mm. Cu
Under the Open Areas, Closed Areas and the Weighted Averages

| Depth in cm. | Area of Field in Square Centimeters | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 100 | | | 150 | | | 200 | | | 300 | | |
| | Open | Closed | Wt. Aver. | Open | Closed | Wt. Aver. | Open | Closed | Wt. Aver. | Open | Closed | Wt. Aver. |
| 0 | 113 | 18.5 | 56.0 | 115 | 21.5 | 59.0 | 116 | 23.0 | 60.3 | 123 | 23.3 | 63.0 |
| 1 | 99.5 | 21.0 | 52.5 | 101.3 | 23.8 | 55.8 | 103.8 | 25.5 | 57.5 | 109.5 | 26.5 | 60.0 |
| 2 | 86.3 | 22.3 | 48.5 | 88.2 | 25.3 | 52.5 | 92.0 | 27.5 | 54.2 | 96.5 | 28.7 | 56.5 |
| 3 | 74.3 | 22.8 | 44.3 | 76.8 | 26.0 | 48.5 | 80.5 | 28.7 | 50.5 | 84.3 | 30.0 | 52.7 |
| 4 | 64.0 | 22.7 | 39.7 | 67.0 | 25.8 | 44.0 | 70.0 | 29.0 | 46.3 | 73.5 | 30.3 | 48.5 |
| 5 | 55.0 | 22.0 | 35.0 | 58.0 | 25.2 | 39.0 | 60.8 | 27.7 | 41.3 | 64.3 | 29.5 | 43.8 |
| 6 | 47.3 | 20.5 | 30.7 | 50.7 | 24.0 | 34.5 | 53.0 | 26.3 | 36.8 | 55.8 | 28.5 | 39.0 |
| 7 | 40.3 | 18.7 | 26.8 | 43.7 | 22.2 | 30.3 | 45.5 | 24.5 | 32.5 | 48.2 | 26.7 | 34.5 |
| 8 | 34.0 | 16.5 | 23.3 | 37.3 | 20.0 | 26.7 | 39.2 | 22.0 | 28.5 | 41.3 | 24.5 | 30.5 |
| 9 | 28.3 | 14.5 | 20.0 | 31.5 | 17.7 | 23.5 | 33.0 | 19.3 | 24.7 | 35.0 | 22.0 | 27.0 |
| 10 | 23.2 | 12.5 | 17.2 | 26.2 | 15.7 | 20.2 | 27.7 | 17.0 | 21.5 | 29.3 | 19.3 | 23.5 |
| 15 | 10.2 | 6.0 | 7.7 | 11.6 | 8.0 | 9.4 | 12.5 | 8.8 | 10.4 | 13.8 | 10.0 | 11.5 |

Mucous Membrane: For the intraoral cases, the epithelitis (pseudo-diphtheritic membrane indicating destruction of the superficial layers of mucous membrane) appeared in ten to fourteen days with tumor doses of approximately 8,000 to 10,000 r under the open areas. The time of appearance of this reaction corresponds to that described by Coutard in 1931 with a dose of about 4,500 $r_0$ to 5,000 $r_0$ to the skin and about 3,500 $r_d$ to the mucous membrane. This suggests that the time of appearance of the epithelitis is independent of the size of the dose, providing sufficient radia-

TABLE III

COMPARISON OF NUMBER OF ROENTGENS DELIVERED WITH A GRID AND WITHOUT A GRID FOR SKIN TOLERANCE IN EACH CASE

10×15 cm. Field, 200 kv., 50 cm. Target Skin Distance, Half-Value Layer 1 mm. Cu
Dosage Protracted over One Month
Tolerance Dose with Grid 24,000 r in Air, without Grid 3,250 r in Air.

| Depth In cm. | No. of r with Grid | | | No. of r without Grid |
|---|---|---|---|---|
| | Open | Closed | Wt. Aver. | |
| Surface | 27,500 | 5,150 | 14,200 | 4,500 |
| 5 | 13,900 | 6,050 | 9,350 | 3,050 |
| 10 | 6,300 | 3,770 | 4,850 | 1,620 |
| 15 | 2,800 | 1,920 | 2,250 | 850 |

TABLE IV

COMPARISON OF NUMBER OF ROENTGENS DELIVERED WITH A GRID AND WITHOUT A GRID FOR SKIN TOLERANCE IN EACH CASE

10×15 cm. Field, 400 kv., 60 cm. Target Skin Distance, Half-Value Layer 3.3 mm. Cu
Dosage Protracted over one Month
Tolerance Dose with Grid 24,000 r in Air, without Grid 4,180 r in Air.

| Depth in cm. | No. of r with Grid | | | No. of r without Grid |
|---|---|---|---|---|
| | Open | Closed | Wt. Aver. | |
| Surface | 25,300 | 4,920 | 13,000 | 5,200 |
| 5 | 13,100 | 6,820 | 9,300 | 3,650 |
| 10 | 6,700 | 4,350 | 5,300 | 2,050 |
| 15 | 3,400 | 2,520 | 2,880 | 1,140 |

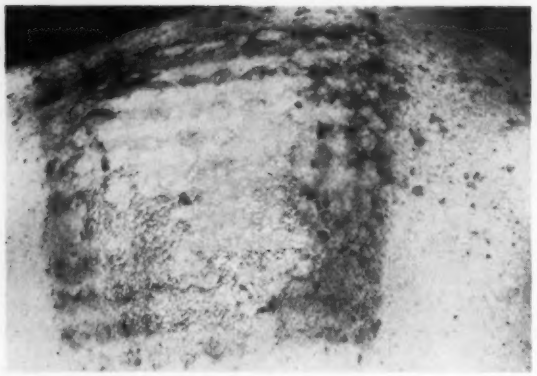

FIG. 5. Height of reaction with moist desquamation of the skin of the treated portal.

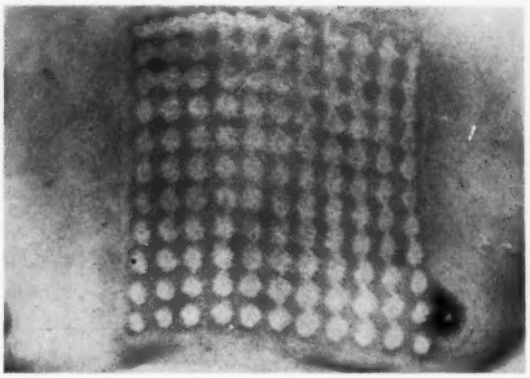

FIG. 6. Final stage in healing of the skin showing depigmentation under the open areas and tanning under the covered regions giving an appearance of a reversal of the grid pattern.

tion is delivered to obtain such a destructive reaction. Healing, however, is much delayed as compared to the Coutard method. Coutard states that healing takes place in about two weeks following the appearance of the epithelitis. With grid therapy, the reaction is more severe and the time period for healing much longer. The shortest period was seven weeks and the longest about four months. Severe intraoral pain was often present with the mucous membrane reaction and persisted in some instances after apparent healing.

### RESPONSE TO THERAPY

The response to therapy is best discussed according to the anatomical site of the primary lesion. This material has been listed in Table 1 and the cases will be referred to by their case numbers.

*Head and Neck.* The 11 cases (Cases 1–11) consisted of 3 cancers of the larynx, 2 of the nasopharynx, 2 of the soft palate, 1 of the buccal mucosa, 1 of the tongue and floor of mouth, 1 of the tonsil and 1 of the antrum. Four patients have died, 1 with the disease clinically controlled, the others with active disease. In the 7 patients still living, 1 is receiving treatment to the metastatic lymph nodes but the primary lesion in the nasopharynx has disappeared. The patient with the lesion in

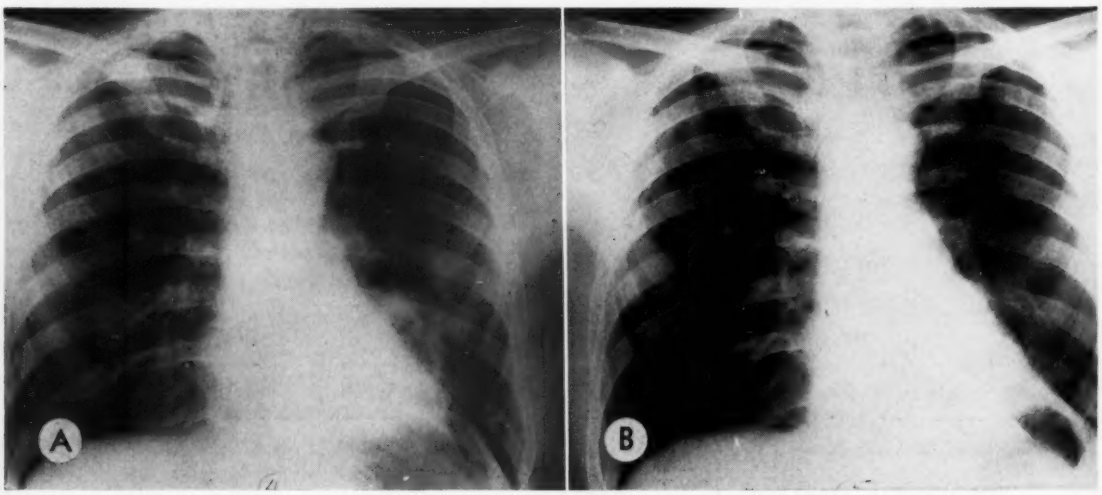


FIG. 7. Carcinoma of the left lower lobe bronchus (R.A., Case 19) (*A*) at beginning of treatment, (*B*) following treatment.

the buccal mucosa shows no evidence of persisting disease but the period of observation is only six months. Two patients, one with the nasopharyngeal carcinoma and the other with a carcinoma of the larynx had striking palliation for short periods. Three patients had temporary palliation but with the primary disease uncontrolled.

*Chest.* The 8 bronchogenic carcinomas (Cases 12–19) were all considered advanced inoperable cases when irradiation was instituted. Four cases still survive although the period since treatment is very short. In 2 of these patients, the primary tumor has receded and there has been symptomatic improvement. The immediate response of R.A. (Case 19) was spectacular. Figure 7*A* shows the tumor at the start of treatment and Figure 7*B* the disappearance of the tumor at conclusion of therapy. The other 2 patients show slight symptomatic relief but the tumor persists. Postmortem examinations were performed on the 4 patients who died. In no instance was the primary tumor eradicated, yet the doses at the site of the growth under the openings ranged from 5,640 r to 7,000 r. The ninth case of intrathoracic neoplasm (Case 20), a patient with metastases following resection of a mediastinal teratoma, showed disappearance of the metastases following irradiation.

*Gynecologic Group.* The 4 cases of ovarian cancer (Cases 21–24) were all far advanced. One patient with extensive pelvic disease and pulmonary metastases had shrinkage of the tumor in the areas irradiated with relief of pain but her condition became rapidly worse and she died. A second patient had shrinkage of the pelvic masses. She also did badly during the period of treatment and died within six weeks. The third patient had pelvic masses plus extensive involvement of the vagina. Bleeding was controlled by the irradiation. The fourth patient had grid therapy following removal of both ovaries and resection of the sigmoid for ovarian carcinoma. The patient showed improvement for six months, after which she had recurrence

TABLE V

COMPARISON OF DEPTH DOSES FOR 2 MILLION VOLT, 22 MILLION VOLT AND 200 KV. ROENTGEN RAYS UNDERNEATH THE GRID CLOSURES IF THE DOSES AT 0.5 CM. DEPTH ARE CONSIDERED 100 PER CENT

| Depth in cm. | 2 mv. 100 cm. T.S.D. 10×10 cm. Field | 22 mv. 105 cm. T.S.D. 75 sq. cm. Field | 200 kv. under Closures. 50 cm. T.S.D. 10×10 cm. Field |
|---|---|---|---|
| 0 | 90% | —% | 96% |
| 0.5 | 100 | 100 | 100 |
| 1 | — | — | 106 |
| 2 | — | 176 | 113 |
| 3 | — | 186 | 116 |
| 4 | — | 186 | 115 |
| 5 | 76 | 186 | 113 |
| 7 | 66 | 163 | 99 |
| 8 | — | 157 | 89 |
| 10 | 52 | 142 | 70 |
| 15 | 36 | 126 | 36 |

for which she received conventional irradiation. The 2 cases with carcinoma of the uterine cervix (Cases 25 and 26) were advanced Stage IV. One patient received only five treatments when therapy had to be discontinued because of peritonitis. This case will be discussed in detail under complications. The other patient had radium and conventional roentgen therapy with rapid progression of the disease. When a dose of 16,200 r in air was reached with grid therapy, she developed an acute intestinal obstruction and irradiation had to be discontinued. The obstruction was relieved by nonoperative procedures but she died soon afterwards.

*Carcinoma of the Bladder.* Three cases are included in this group (Cases 27–29). One patient who received grid therapy after biopsy and fulguration of the primary lesion is now free of disease for ten months. Another patient with extensive involvement of the bladder complicated by pyelonephritis in the remaining kidney (the other had been resected at an earlier date) had control of pain at completion of treatment but died one month later of pyelonephritis and uremia. The postmortem

examination revealed persisting necrotic carcinoma in the bladder. The third patient improved with conventional roentgen therapy for about eight months. He was then given grid therapy for recurrence. The bladder was negative on cystoscopic examination, three months after treatment. He suffers severe suprapubic pain due to radiation skin necrosis. This case will be discussed in detail under skin complications.

*Carcinoma of the Gastointestinal Tract.* Four patients (Cases 30–33) composed this group. One patient with advanced adenocarcinoma of the stomach died about three months after treatment, unimproved. A second patient with an extensive carcinoma of the stomach with metastases showed no improvement. The patient with the carcinoma of the mid esophagus had a complicating cerebrovascular accident and because of the resulting paralysis could be treated only over one portal. The postmortem examination three months after the irradiation showed no irradiation changes in the treated area. The last patient had local recurrence and metastases to the bladder about three years following abdominoperineal resection for carcinoma of the rectum. He was not improved with conventional roentgen therapy or with grid therapy two months later.

*Miscellaneous.* Case 34 had metastases to the left supraclavicular region one year following left radical mastectomy for carcinoma of the breast. Following grid therapy the metastases disappeared and the patient is free of disease up to the present, fifteen months after irradiation. The skin shows some atrophy and pigmentation and an indistinct grid pattern but is supple. The clavicle was protected by a thin strip of lead rubber and shows no irradiation changes.

The patient with Hodgkin's disease (Case 35) had had a laminectomy followed by a course of radiotherapy at the level of D8 and D9 because of compression of the spinal cord by an extradural mass. After ten months, a large mass was discovered which filled the left lower pelvis and disappeared following grid therapy. Six months thereafter, necrosis of the skin developed in the region of the groin. This complication will be discussed in greater detail in the next section.

## COMPLICATIONS

*General.* Although the results in our advanced cases are not exceptional, they are sufficiently promising to warrant a further trial with earlier cases more suitable for irradiation. Since this method will be coming into more general usage, it is important for radiologists to be aware of the complications which may be encountered with this technique. The general reactions are similar to those of conventional roentgen therapy but are more severe and of longer duration. They are particularly marked in the head and neck cases and in patients treated over the abdomen. The head and neck group, due to severe and persistent mucous membrane reactions, suffer anorexia and dysphagia for such long periods that maintenance of good nutrition becomes a problem difficult to cope with. Several patients, particularly those in the older age group, required hospitalization for gastric tube and parenteral feeding. In one case these measures did not suffice and the patient died apparently from inanition, although the disease was clinically controlled.

Local complications will be considered under the organ or system involved.

*Skin.* Previous Irradiation: Where the skin has received intensive irradiation, and grid therapy is applied subsequently because the disease has not been controlled, there is danger of skin necrosis. Dosage and the portal to be irradiated should be kept as small as possible.

J.J. (Case 28), a male, aged forty-seven, with carcinoma of the bladder (Table 1) had received a skin dose of 4,000 $r_0$ with 400 kv., to each of two anterior suprapubic portals. Prior to this irradiation, suprapubic cystotomy had been performed. He was improved for approximately four months when he developed recurrence of symptoms. Cystoscopy and biopsy

three months later showed recurrence of the carcinoma. Control of the disease could not be hoped for with further conventional radiotherapy and it was decided to treat this patient through a grid though the danger of skin breakdown was grave. Four hundred kilovolts was utilized to spare the skin as much as possible. He was given 20,500 r in air to a 10 by 10 cm. suprapubic field over a period of four weeks. The epidermitis which followed was very severe and has not healed up to the present. He suffers great pain and is extremely uncomfortable as a result of the skin necrosis. Dysuria and difficulty in starting the urinary stream are much improved. Cystoscopy three months following the irradiation showed contraction of the bladder with inflammation of the mucosa and apparent disappearance of the neoplasm.

Large Portal: The chances for radiation necrosis in the treated area are greatly increased the larger the portal irradiated.

M.M. (Case 35) is a male aged fifty-four. Mention was made of this patient under the discussion of local skin reactions. About ten months following laminectomy and conventional radiotherapy for epidural tumor at D8 to D10, proved to be Hodgkin's disease, he developed a large mass which filled the left lower pelvis. A dose of 6,800 r in air was given through a grid over one large anterior portal 20 by 15 cm. The field was then decreased to 15 by 14 cm., and therapy continued to a total dose of 16,200 r in air over a period of four weeks. The resulting epidermitis was completely healed in seven weeks. Three months later thickening was noted in the skin in the treated area, particularly in the groin. Six months following the irradiation, necrosis appeared in the skin just above the groin. At present, nine months following irradiation, the necrotic skin is healing slowly. It is probable that the continuous trauma to which the skin of the groin is subjected was an important factor in the production of the necrosis. Size of portal was a likely factor in the initial damage the skin sustained.

*Mucous Membrane.* For the head and neck group epithelitis was accompanied by edema, severe pain and anorexia. Persisting dysphagia due to the slow healing of the epithelitis causes disturbance of nutrition in some patients. In other instances, there

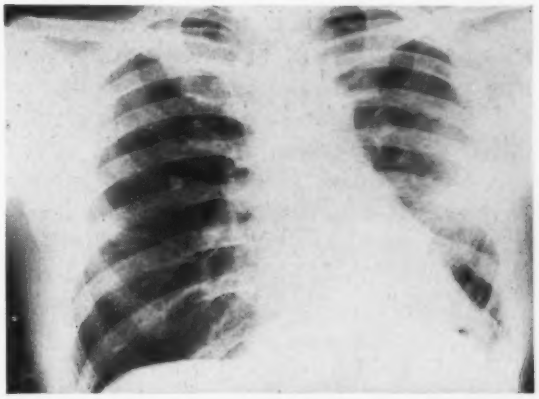

Fig. 8. Radiation pneumonitis left lung eighteen days following completion of the treatment (R.A., Case 19).

is danger of early or late radiation necrosis of the irradiated area.

N.S. (Case 2), a carcinoma of the left buccal mucosa, has complained of severe pain in the region of the left cheek since completion of his treatment. At present, six months later he shows a small area of necrosis in the mucous membrane of the irradiated left cheek.

Carcinomas of the head and neck regions are usually close to the surface. It is inadvisable to give irradiation to the limit of skin tolerance (20,000 to 24,000 r). An adequate tumor dose can be obtained with less irradiation. The resulting skin and mucous membrane reactions will be less severe and the danger of necrosis greatly diminished.

*Bone and Cartilage.* Complications were not present which were referable to bone and cartilage. None of the cases treated for pulmonary carcinoma developed an osteochondritis of the ribs. In 2 patients with intensive irradiation over the ear, the skin reaction was unusually severe with epidermitis, pain and marked swelling of the auricle. Both patients developed infections of the external auditory canal superimposed on the epidermitis. Healing of the ear was delayed but subsequently the skin healed and the pain and swelling disappeared. The symptoms were thought to be partially due to complicating chondritis, not proved because healing was complete. When giving grid therapy for nasopharyngeal and

intraoral disease, it is advisable to protect the ear, if possible, to avoid reactions of this type.

*Urinary Bladder.* Patients develop a radiation cystitis when treatment is given over the bladder. The resulting symptoms have not been of such severity as to interfere with the planned irradiation. The cases treated over the bladder have been few and were not followed long enough to determine if late changes take place.

*Bowel.* Grid treatment over the lower abdomen, especially if the portals are large, is usually accompanied by diarrhea. In an occasional case where drug therapy has failed, irradiation must be discontinued to control the frequent bowel movements, tenesmus and nausea. Injury to the large intestine such as described for intensive conventional therapy may be encountered.

E.P. (Case 21) was a female, aged forty-five, with postoperative cystadenocarcinoma of the ovaries with widespread abdominal involvement. In March, 1939, a hysterectomy and subtotal oophorectomy had been performed for fibroids and "ovarian tumor." The patient was asymptomatic for eight years when a mass filling the pelvis was discovered and removed in July, 1947. The diagnosis was cystadenocarcinoma of the right ovary. Surgery was followed by intensive irradiation. In October, 1949, another laparotomy was done for removal of tumor tissue. She was admitted to the Montefiore Hospital nine months later for further irradiation. A total of 16,400 r in air was given over a period of five weeks to an anterior pelvic portal 15 by 20 cm. Therapy in this case was interrupted several times due to diarrhea accompanied by nausea and vomiting. Although the ascites decreased and the local mass became smaller, the general condition of the patient deteriorated rapidly and she died two weeks following completion of the irradiation. The postmortem examination revealed a 3 by 3 by 4 cm. tumor mass in the right pelvis with necrosis and cellular distortion thought to be due to irradiation. There were 3 by 5 cm. ulcerations in the sigmoid and caecal regions; both of these areas were in the field of irradiation. The ulcerations were irregular, moth-eaten, and showed bridges of relatively intact mucosa traversing patches of superficial ulcerated and reddened granulation tissue. Microscopically, these ulcerated areas showed eosinophilic necrotic material which was fibrillary and interspersed with granular detritus extending deep into the muscularis. Cytoplasmic vacuolation and nuclear distortion was present in varying degrees. The changes were considered a radiation effect.

*Infection.* Low grade pelvic inflammation can be activated by irradiation. Prior to the use of antibiotics great caution was exercised in treating over the pelvis for gynecologic carcinoma in order to avoid the breakdown and generalized spread of a walled-off infection.

B.L. (Case 25), a female, aged fifty-nine, with a Stage IV squamous cell carcinoma of the cervix, was admitted to the Tumor Clinic for irradiation. Treatment was started with the grid. The initial dose was low, only 600 r in air. No reaction followed and the dosage was increased to 1,200 r in air. Bleeding was controlled after the second treatment. Following the fifth treatment, she developed severe abdominal pain, chills, nausea and urinary difficulty and a temperature of 104° F. She was admitted to the hospital with symptoms and signs of peritonitis believed due to lighting up of a latent pelvic infection. She responded to antibiotics, parenteral fluids and decompression of the bowel. After about five weeks, the patient was sufficiently improved for irradiation to be resumed. She was given conventional irradiation so that small doses could be used which would be less likely to activate persisting pelvic infection. She died five months following completion of this treatment. At the postmortem examination the pelvic space was walled off by adhesions of small and large intestine. A recto-vesicovaginal fistula formed a cloaca-like space into which the left ureter drained. Pelvic walls were lined by green necrotic material which also communicated with the cloaca. Tumor persisted in the pelvis.

*Lung.* The dosage that is necessary to control intrathoracic neoplasms is such that radiation pneumonitis is a possible complication. Of the 9 cases receiving pulmonary irradiation, 2 developed such a reaction.

M.T. (Case 17) is a male, aged sixty-three,

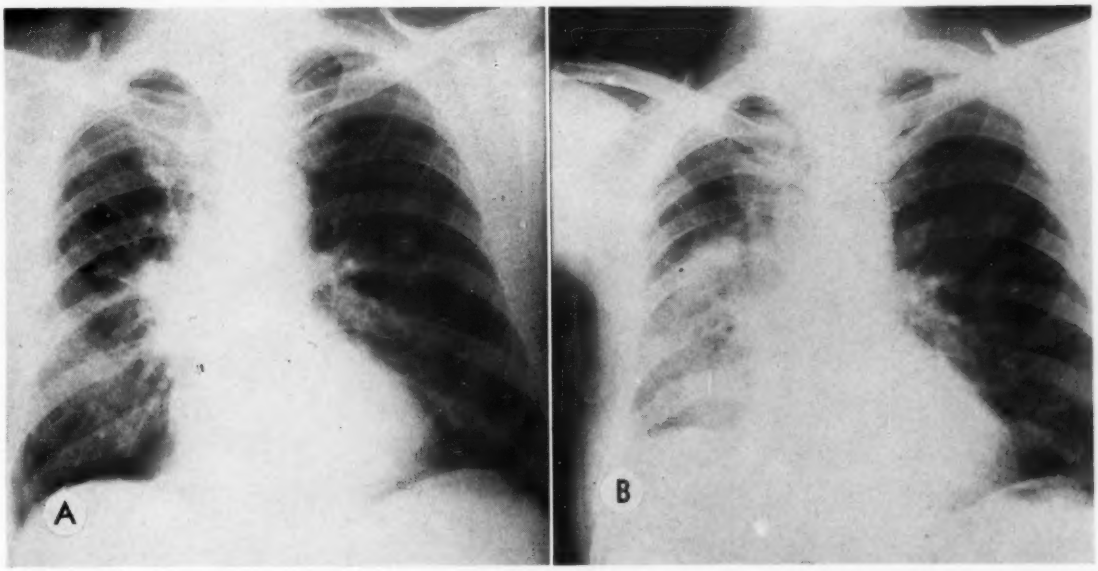


FIG. 9. M.T., Case 17. Bronchogenic carcinoma of the right middle lobe (*A*) at the beginning of treatment, (*B*) radiation pneumonitis following treatment.

with a bronchogenic carcinoma of the right middle lobe bronchus. He received 2,400 r each over anterior, posterior and lateral portals (200 kv.). This was followed by temporary improvement. He was referred to Montefiore Hospital four months later because of recurrence. Grid therapy was started over anterior and posterior portals 12 by 15 cm. and 13 by 15 cm. respectively. He received 16,800 r in air to the anterior portal in three weeks, followed by 11,200 r over the posterior portal in four weeks. The tumor dose was calculated to be 5,030 r under the open areas. Four weeks later beginning pneumonitis was observed in the irradiated lung (Fig. 9, *A* and *B*). It is very likely that damage to the lung resulting from the first course of irradiation, even though not demonstrable on the roentgenogram, was a factor in the production of the pneumonitis which followed the grid therapy. Similar changes have been described by one of the authors (J.R.F.). in a previous publication.[1]

The second case, R.A. (Case 19), a male aged forty-eight, who had a carcinoma of the left lower lobe bronchus, was given 13,400 r over an anterior portal measuring 15 by 12 cm. in six weeks and 10,700 r to a posterior portal 15 by 12 cm. in three weeks. The calculated tumor dose under the openings was 5,990 r. During the period of irradiation, he developed difficulty in swallowing and roentgenograms showed a perforation of the posterior wall of the esophagus opposite D7 and D8 (Fig. 10*A*). The irradiation was continued and fortunately the esophageal perforation healed without producing sequelae (Fig. 10*B*). Radiation pneumonitis was demonstrable eighteen days following completion of the treatment (Fig. 8).

It is well known that massive doses, especially if repeated, are likely to produce radiation pneumonitis. Our experiences with the treatment of pulmonary carcinoma by conventional roentgen therapy, as well as the positive findings in the two cases cited, suggests that when irradiating the lung with the massive single and large total dosage used in grid therapy, radiation pneumonitis is a possible sequela. Portals should be kept as small as compatible with the size of the lesion being treated. The mediastinum should be avoided wherever possible to limit damage to vital structures. Pneumonitis of mild degree will probably heal without permanent symptoms.

## DISCUSSION

The majority of patients constituting this report had far advanced disease. Yet some of the results in the head and neck, pulmonary and bladder groups were promising. It is very likely that greater success

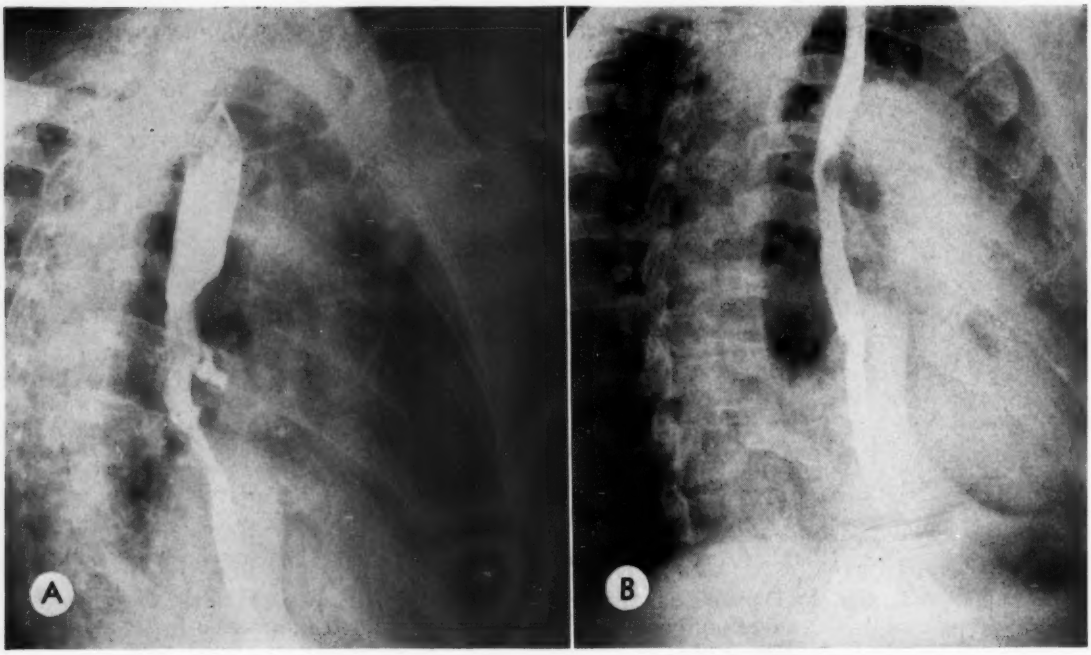


FIG. 10. R.A., Case 19. (*A*) Perforation of the esophagus at the level of D7 and D8; (*B*) healing following irradiation.

will follow the use of this method of irradiation for suitable earlier cases particularly the head and neck, pulmonary, esophagus and bladder neoplasms. Until more reports are available, one should exercise caution in the selection of cases for treatment with due regard for the complications that may be encountered.

At the present time no reasonable explanation can be given for the greater skin tolerance with grid therapy. The skin under the covered areas receives about the same radiation dose as in conventional therapy and under the holes receives about five times this amount. The difference in quality between the direct radiation and the stray radiation might account in some part for the differential reaction. A further investigation will have to be made to measure the half-value layers of the direct and scattered beams at various depths.

It seems hardly possible that the improved healing is due to the nonuniformity of the irradiation.

The disappearance of tumors at a depth, however, can be explained by the greater dose which can be delivered with grid therapy. The depth dose is greater because the dose delivered to the skin is larger; therefore, even though the holes are small, the radiation reaching a depth is more than in conventional therapy. Under the covered part the dose increases over the skin dose to a depth of from 7 to 9 cm. In conventional therapy the skin dose is the same but the dose falls off continuously with the depth.

It would be of great interest to study the pathologic effect on tumors in large animals treated with the grid in order to find an explanation for the differential reaction between the surface and the depth.

## SUMMARY

1. The technique of roentgen therapy through a grid is described.

2. The air dose, skin and tumor doses under the open and closed parts of the grid are tabulated for the thirty-five cases treated.

3. A table of depth doses for different sizes of fields is given.

4. A comparison is made between the doses delivered with a grid and without a grid for skin tolerance.

5. Supervoltage radiation is compared with the radiation under the covered part.

6. The local and general reactions encountered with grid therapy are described.

7. The therapeutic response for the cases treated is given.

8. The complications encountered are discussed.

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DISCUSSION

Dr. Hirsch Marks, M.D., New York, New York. Knowing Dr. Freid as a meticulous radiotherapist with whom I worked at the Cancer Institute under the direction of Dr. Maurice Lenz, the excellent paper presented by him in collaboration with his co-workers, Miss Lillian Jacobson, physicist, and Dr. Lipman, is doubly important because it is both thorough and instructive.

I shall limit my discussion to a brief résumé of the grid technique, stressing some of the clinical and physical aspects gleaned from my own experience with it over a period of eight years.

Advanced carcinoma of large volume was found to respond more readily when roentgen radiation is applied through a lead-rubber grid as adequate quanta of roentgen rays can now be delivered safely across the barrier of normal tissues. Thus, because by reducing the volume of tissue irradiated, we greatly limit absorption of secondary radiation in the skin, thereby raising the rate of transmission. The grid technique is based largely on the delivery of optimum doses causing lysis of the tumor, but from which the normal tissues will readily recover. The recovery factor is inherent in the permanently protected skin areas in which healing is initiated and extends to the bordering opaque

squares or circles, because no roentgen rays reach these covered areas directly through a lead-rubber grid 8 mm. in thickness, except what is scattered back by roentgen-ray diffusion. The total dosage corresponding to the size of the field, in irradiation through a grid, is predicated on a maximum safe dose, *i.e.*, 2,500 r in air, which the covered areas will readily tolerate without undergoing permanent changes in the blood supply upon which the whole mechanism of healing is dependent.

Upon this latter fact, as well as other potent clinical considerations—nutritional status, anemia, infection—will depend the ultimate success of treatment with this method. The selection of the dose will therefore be gauged by its relative effect on the normal tissues which must remain inviolate under all circumstances. Changes in blood vessels and lymphatics causing obliteration of their lumens, thereby plugging up the channels through which tumor debris is removed, are disastrous when they occur in the process of irradiation. These facts should be borne in mind especially in cases of deep-seated tumors where the cross-fire method is recommended for these reasons.

To avoid these pitfalls the local and general systemic reactions of the patients must be the guide posts in determining the size of the dose and the intervals of treatments. It is therefore incumbent on a radiotherapist to observe all patients under treatment with a grid very closely. In other words, roentgen therapy through a grid is not an a priori devised plan which you follow irrespective of the local and general condition of the patient. We cannot stress too emphatically the importance of the presence of a trained radiotherapist at each treatment. Roentgen therapy through a grid must never be carried out by prescription handed to a technician. The local and general response of the patient to treatment must be evaluated on a day-by-day basis by a trained radiotherapist.

Regarding the nausea, vomiting, diarrhea, and dysphagia which occurred rather frequently in some of the cases presented, these factors may mean a difference between obtaining good palliation and no palliation at all.

In my experience, these symptoms occurred in less than 3 per cent of the 200 cases treated. However, I wish to emphasize for the benefit of those who are using this method that we aimed from the beginning to establish a better nutritional status by administering essential amino-acids and therapeutic doses of vitamins and, in those sites where infection is usually present, like the bladder and throat, we also administer antibiotics as soon as treatment is instituted. I would also suggest that, wherever possible, the size of the field should never exceed 10 by 15 cm. and in cases of larger tumors, offering an uneven surface, two adjacent fields may be used with better results.

DR. J. A. DEL REGATO, Colorado Springs, Colorado. Dr. Freid and his collaborators are to be congratulated for this very interesting and scholarly report. I would like to enter in the record the fact that Coutard intermittently experimented with this form of irradiation as far back as 1924 and as recently as 1949. Because, among other things, he did irradiate patients through holes, unkind comments were made about his sanity. As we have seen, the method permits a relatively larger depth dose and thus becomes what has been called a sort

FIG. A. Patient treated by Coutard for a histopathologically proved carcinoma of the left breast through a grid in 1942. Photograph taken in 1951. The irradiation was tangential; this explains the confluence of telangiectasis towards the midline, since the grid was not on the patient.

of "poor man's supervoltage." Coutard was not concerned with depth dosage, however; he was interested in the possibility of affecting tumors with less damage to surrounding vasculo-connective tissue. In the past three years I have repeatedly examined a woman treated by Coutard in 1942 for a histopathologically proved carcinoma of the breast; she now has spotted

areas of atrophy and telangiectasis, but appears to be free from recurrence (Fig. A). Coutard did not use a perforated rubber mat, but a perforated lead piece which was placed on the tube-head just below our lighting localizer.

I, myself, have never tried any form of "Swiss cheese" radiotherapy. I would like to suggest that a lead disc with concentric perforations may be made to rotate in the beam of rays during the irradiation; the result would be a series of concentric areas of directly irradiated and non-directly irradiated tissues in the coniform path of radiations; perhaps this would be worthy of a physical study.

Dr. William Harris, New York, New York. Since early in 1950, we have had some experience with this method. We have treated 149 patients and have completed the treatment as of September 1, 1951, on 127 patients. These were all hopeless cancer patients, either for conventional radiotherapy or surgery and were treated for palliation.

This modification of the grid method was called to my attention by Dr. Hirsch Marks and, if there is merit in it, I believe that he has made the most significant recent contribution for renewed interest in its use.

I do not believe that anyone should treat a patient with cancer with this method unless it is considered hopeless by a radiotherapist, a clinician and a surgeon, and that no one should assume this responsibility on his own if dosage such as has been suggested today is to be employed. I do not believe that it is safe to give a patient 24,000 r through a single portal with a grid in a twenty-eight day period if the patient has a life expectancy of much over a year. We have treated 16 patients with 24,000 r and I believe now that this dose is excessive.

In our limited experience we believe that the best palliation has occurred in advanced pulmonary and bladder cancers. Among the 35 lung cancers treated up to September, 1951, two with positive carina biopsies were operated on after grid therapy and the specimens confirmed the post treatment bronchoscopies that the carinas and main bronchi were clear of disease. Residual disease in the lungs was found in both cases. A more recent patient shows similar sterilization of the carina following treatment but this has not been confirmed by surgery. Another patient had a pneumonectomy after grid therapy and the excised lung showed no histological evidence of cancer. Among the other patients in this group palliation was obtained in most cases in the control of hemorrhage, cough and pain.

One year ago a patient with a pelvic desmoid (benign fibrosarcoma) was referred for treatment. Recurrence with extension to the iliac vessels, edema of the leg and pressure on the rectosigmoid followed two excisions and conventional radiotherapy. The patient was advised to have a hemipelvectomy. This was refused. Radiotherapy through a grid was given after the patient and her family were warned that the method was experimental and that nothing could be hoped for by radiotherapy. Our most recent follow-up, much to our surprise, showed the disappearance of the extrarectal mass, diminution of the edema of the leg and lessening of the pain.

Physical measurements indicate an advantage in depth dose with this method when compared to conventional open port therapy if doses are carried to normal tissue tolerance. However, our experience is still too limited in time to ascertain the late sequelae. For this reason, dosages such as were suggested in the previous paper must be employed only in proved hopeless cancers. We believe that this method is simpler to apply than conventional rotating or multiple field therapy with 200 kv. and is often less taxing on the patient.

Dr. Maurice Lenz, New York, New York. The authors have presented a most unbiased and carefully analyzed study of their experience with grid therapy at Montefiore Hospital, New York. I believe they have recently reached the same conclusion as I have regarding daily dosage: I rarely administer more than 500 r in air daily to a field of 6×8 cm. or larger through a grid, if the total air dose is 10,000 r or more; the late radiation changes in normal tissues otherwise are too severe.

Dr. G. Failla, New York, New York. It seems to me that the use of the grid is a good thing provided it is not carried to excess. I believe that when the proponents use doses of 24,000 roentgens in air, they are carrying this to excess, because under these conditions, the skin, even under the lead rubber, receives as much radiation as it does from the ordinary open port therapy with 3,300 r in air. Therefore, the shielded skin and tissues underneath are damaged to the same extent that they are with a much smaller dose through an open port. In

addition to that, the tissues that are exposed through the holes, are damaged to a much greater extent. So the two treatments cannot be equal as far as normal tissue damage is concerned. In other words, the grid treatment of 24,000 r must be more severe to the patient than the open port treatment of 3,300 r. There should be no question about that.

The basis for grid therapy is the biological observation that recovery can take place more readily in a mass of tissue when small regions of heavily irradiated tissue are surrounded by regions that have received less radiation and therefore have not been severely damaged. However, if this is true for normal tissues, it must also be true for the tumor. Accordingly, to take full advantage of the method one should make sure that as much overlapping of beams as possible occurs in the tumor while at the same time there is the least overlapping in the intervening normal tissues.

When the tumor is at a depth of more than 10 cm., the radiation is distributed fairly uniformly within it, because scattered radiation causes considerable overlapping of the beams. Also, when numerous treatments are given over the same area (even with perfect registry of the grid on the skin), the direction of the beam is apt to vary some, and overlapping is facilitated. Actually an effort should be made to change the direction of the beam with respect to the grid at each treatment in such a way as to obtain the maximum overlapping in the tumor without causing too much overlapping in the intervening normal tissues. This can be done effectively only in the case of very deep-seated tumors. I cannot see how there can be any real advantage in using the grid technique for the treatment of neck cases. I would expect, therefore, that the clinical results in neck cases obtained with the grid scheme would not be appreciably better than those obtained with treatments through open ports, when the doses are such that the same amount of local as well as systemic damage is produced by the two techniques.

MISS LILLIAN E. JACOBSON. There is a great deal that we cannot answer about this, but I do think that this method is good in head and neck cases because underneath the covered area there is an increase in the depth dose to about 3 cm., that is an increase over the skin dose, after which the dose levels off and then comes down. Whether it is the portion underneath the covered area or whether it is the portion underneath the open area that is instrumental in causing the result, we don't know. I think it is a little dangerous to try to angle the tube differently, on purpose, because you are apt to injure the skin which you are trying to save.

There is another thing which I would like to bring out and that is, in trying to save the skin, you want to place the grid over the same area all the time. If you use a thick grid or a lead grid, as we have with the 400 kv. work, you cannot always position it over the same openings because these grids are not pliable and do not make good apposition with the skin, and you are apt to have radiation which came through a hole before, now over a covered part, or vice versa. In other words, you are covering the whole area on the skin with radiation, which you want to avoid. Therefore, the more pliable the grid, the better I think it is. I cannot see the advantage in having a thick grid which perhaps allows 0.8 per cent of radiation to go through the covered part rather than a grid which is half that thickness, which will allow 1 per cent or 1.5 per cent of the radiation to go through. I don't think that amount of radiation going through the covered part makes much difference.

DR. FREID (closing). This presentation is intended to inform those contemplating giving irradiation through a grid of some of the complications that may be encountered. Radiation through a grid is coming into more general usage and unless radiotherapists are cognizant of possible complications, many patients will receive radiation injuries. Although initially up to 24,000 r in air were given to single ports, we now believe such a dose to be excessive and that 15,000 r per port is safer. The daily dose has been cut from 1,000 to 1,200 r in air to 600 to 800 r in air. The treatment period has been extended from four to five weeks to about six to seven weeks.

Dr. Failla has suggested that the tube be angled so as to obtain increased irradiation under the covered areas. Such a procedure is contrary to the theoretical considerations underlying this method of treatment.

We believe that radiation given through a grid offers distinct advantages over conventional irradiation for properly chosen cases.

VOL. 70, NO. 3

# THE TOXICITY OF POLONIUM 210 IN MICE

## I. THE THIRTY DAY $LD_{50}$, RETENTION, AND DISTRIBUTION

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### INTRODUCTION

THE first report of the biological behavior of polonium was published in 1913 by Ferneau *et al.*,[3] who found that prolonged exposure of human and rabbit skin to large doses of polonium did not result in the local erythema that followed similar exposure to radium. Since 1924 Lacassagne and his associates[6–13] have been studying the excretion, distribution, and pathological effects of polonium injected into rabbits and rats. They have reported that excretion occurs principally via the kidneys and that the retained material is fixed chiefly in the cells of the reticuloendothelial system. The highest concentration of polonium was found in the spleen, other lymphoid tissues, and renal cortex; the renal medulla and osseous tissue contained only trace amounts. Pathological changes were correlated with the concentration of polonium and cellular sensitivity to irradiation. The injection of lethal amounts was followed in six to twelve days by the destruction of the blood-forming organs and a fatal hemorrhagic syndrome, or by acute nephritis. Lower doses resulted in chronic renal or intestinal inflammation two to four months later.

In 1950 Fink and his co-workers[4] determined the acutely lethal level, the retention, and the distribution of intravenously administered polonium in rats. They found that 50 μc./kg. killed 50 per cent of the animals in twenty days and that retention (including loss by radioactive decay) was 70 per cent at ten days and 17 per cent at 100 days. Casarette[2] described the hematological and histopathological changes that occurred in rats up to 160 days after the intravenous injection of 10 and 20 μc./kg. of polonium.

The establishment of a permissible level of polonium exposure entails investigation of the long-term effects of low doses. This type of study requires a large number of individuals since the latent period for the appearance of pathological changes may approach the life span of the animal. For this purpose the mouse has proved to be a very suitable laboratory mammal. Before long-term studies of the toxicity of polonium in mice could be undertaken, it was necessary to determine certain facts for this species that already have been established for the rat, *e.g.*, the acutely lethal dose of polonium, the rate at which the injected material disappears from the body, and the selective uptake by the various organs. The results of these investigations are reported in this paper.

### EXPERIMENTAL PROCEDURE

Polonium 210 (radium F) has a half-life of 138 days and decays by the emission of an alpha particle and a gamma ray with respective energies of 5.3 and 0.77 mev. It was injected into a tail vein in 0.3 ml. of hydrochloric acid solution in isotonic saline at pH 2.

Seventy-four CF#1 female mice, which were sixty-two to sixty-eight days old and whose average weight was 22 gm., were randomly distributed into the groups shown in Table 1. It was estimated from the results of other workers that the dose that would kill 50 per cent of the animals in thirty days (30 day $LD_{50}$) would fall between 50 and 100 μc./kg. Therefore, animals of groups 1 and 2 were permitted to live until death occurred. Group 3 was selected for the separate analyses of the following: liver, spleen, kidneys, ovaries, mesenteric lymph node, lungs, femur including marrow, gastroc-

* With the technical assistance of Thomas J. Mulhaney.

TABLE I

MOUSE GROUPS

| Group | Dose Level (μc./kg.) | Number of Animals | Disposition |
|---|---|---|---|
| 1 | 100 | 15 | Total body analysis at natural death |
| 2 | 50 | 15 | Total body analysis at natural death |
| 3 | 25 | 15 | Organ analysis at timed intervals |
| 4 | 10 | 15 | Total body analysis at timed intervals |
| 5 | 5 | 14 | Total body analysis at timed intervals |

nemius muscle, and remaining carcass. Groups 4 and 5 were used to study retention over a longer period of time and to compare retention at different doses. The animals were killed with intravenous Nembutal®.

### ANALYTICAL PROCEDURE

Polonium determinations are complicated by the adsorption of the material on glass, colloid formation, and the volatility of many of its compounds above 300°C. The analytical procedure developed for the present study was designed to reduce these complicating factors to a minimum. Since, under proper conditions, polonium spontaneously plates from acid solution on metals such as copper, iron, and silver, it usually is assayed by measuring the alpha-ray activity of a plated disc. Silver was used in these studies because of its relative inertness to hydrochloric acid and because of its availability in thin foils.

The animals or organs to be assayed were placed in Kjeldahl flasks. A minimum of 2.5 ml. of concentrated perchloric acid, or 2.5 ml. for each gm. of tissue, was added. Superoxol ($H_2O_2$—30 per cent Merck) equal to one-half the volume of perchloric acid and water equal to one-fifth the volume of perchloric acid were then added, and the flasks were shaken briefly. After forty-eight hours, during which time preliminary decomposition occurred, the flasks were placed on a digestion rack and maintained at 200°C. In two to twenty minutes the solutions became clear except for an oily layer on the surface. After further heating they became black and started to fume. One to 2 ml. of superoxol was added immediately whenever this occurred; digestion was considered to be complete when a clear white to yellow solution remained that did not blacken on further heating. Total digestion required fifteen minutes to ten hours, the time depending upon the size and fat content of the sample. The cooled solutions were transferred to volumetric flasks and brought to 1N with hydrochloric acid.

An aliquot that was estimated to contain approximately 0.01 μc. of polonium was placed in a 100 ml. round bottom centrifuge tube, and sufficient 1N hydrochloric acid was added to bring the volume to 50 ml. A clean, bright, silver disc, 1 inch in diameter and 0.002 inch thick, was placed in the vessel for the plating of the polonium. The solution was stirred at such a rate that the disc rotated on edge while the tube was heated in a water bath at 90–100°C. After two and one-half to three hours the disc was removed, washed with water, and allowed to dry. Both sides were counted in a standard parallel plate alpha chamber at 52 per cent geometry;[5] the sum of the counts of the two sides was taken as the total count. Similar discs that had been plated from aliquots of the injection solutions were counted at the same time and used as standards.

Sixteen mice were processed by the analytical procedure described above, and mean recovery was found to be 100±2.8 per cent (S.D.).

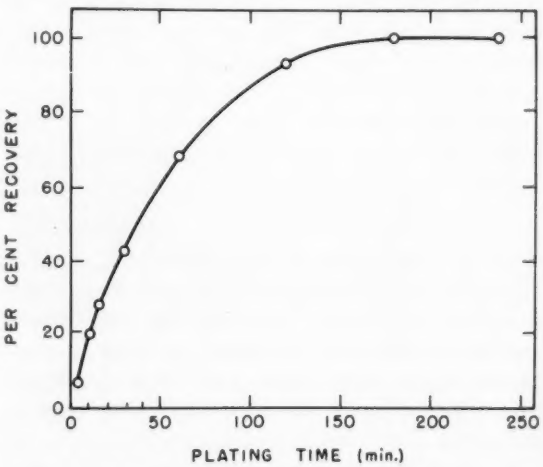


FIG. 1. Recovery of polonium from hydrochloric acid solution as a function of time.

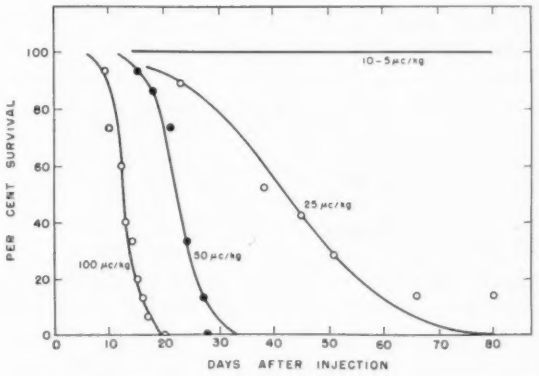


FIG. 2. Survival of CF#1 female mice following the intravenous administration of polonium 210. The percentages were corrected for those animals taken for time-serial sacrifice at the 25 μc./kg. level.

Ashing in sulfuric acid proved to be unsatisfactory because it required temperatures in excess of 200°C., which resulted in loss of polonium by volatilization. Plating was found to be equally good from hydrochloric, sulfuric, and phosphoric acids, but nitric and perchloric acids were inferior, probably because they tended to dissolve the silver disc. The concentration of acid in the plating bath was not critical from 0.01N to 6N. The plating time required for 100 per cent recovery from 50 ml. of solution was determined by removing the silver disc from the solution and counting it at intervals during a four hour plating period. Complete recovery was attained in less than two and one-half hours (Fig. 1). Larger volumes of solution required longer plating times so that complete recovery from 500 ml. of solution required about four days.

## EXPERIMENTAL RESULTS

*Survival.* The survival data plotted on probit paper were found to approximate closely the normal probability function. The curves that were derived from the probit graphs and the actual survival points are presented in Figure 2. All the animals that had received 5 or 10 μc./kg. lived until their specified sacrifice dates. In Figure 3 the logarithm of the number of days to 50 per cent mortality is plotted against the logarithm of the dose. This curve places the thirty day $LD_{50}$ of intravenously administered polonium 210 between 30 and 40 μc./kg. for CF#1 female mice.

*Effect on Body Weight.* At the time the mice were injected with polonium they had not attained full size and were growing rapidly. Those groups that received more than the thirty day $LD_{50}$ (50 and 100 μc./kg.) lost weight precipitously after the first week; those that received 10 or 25 μc./kg. failed to grow during the period of observation; those that received 5 μc./kg. progressed almost as well as 120 control animals that had received intravenous injections of a comparable volume of isotonic sodium chloride solution brought to a pH of 2 with hydrochloric acid.

*Retention.* The percentage of the injected dose that was retained appeared to be independent of the dose level over the range studied. A representative sample of the data is given in Table II. It was therefore possible to combine the various doses for the establishment of the retention curve presented in Figure 4, where the individual values plotted semilogarithmically are adequately represented by a straight line after an initial rapid drop of approximately 20 per cent during the first three days. After this initial drop the biological half-period, when reduction by both excretion and radioactive decay are considered, was thirty days.

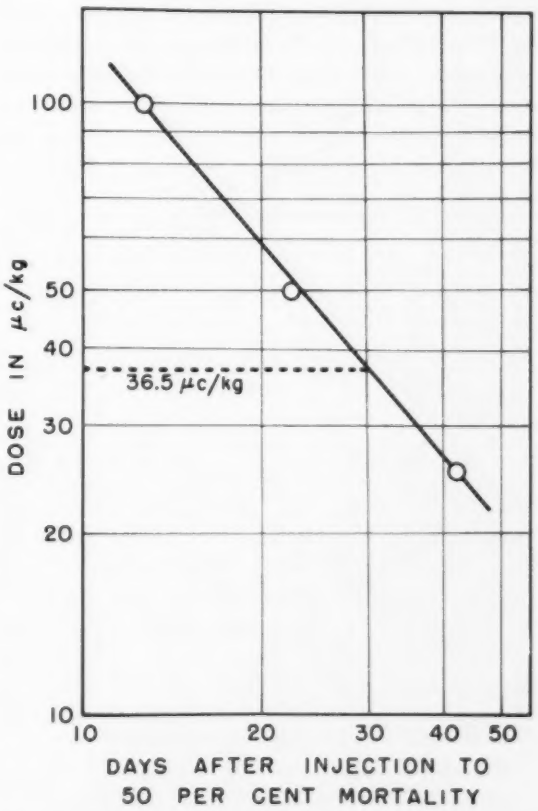


FIG. 3. Dose and interval to 50 per cent mortality.

TABLE II

PER CENT OF VARIOUS INJECTED DOSES RETAINED

| Dose (μc./kg.) | Days After Injection | | | |
|---|---|---|---|---|
| | 3 | 10 | 30 | 120 |
| 100 | | 65.9 | | |
| | | 62.3 | | |
| 25 | 83.4 | 66.8 | 45.4 | 7.9 |
| | 81.9 | 63.5 | 43.7 | |
| 10 | 89.6 | 85.2 | 55.8 | 17.3 |
| | 88.6 | 62.9 | 51.5 | 11.8 |
| 5 | 85.5 | 66.5 | 42.5 | 12.9 |
| | 70.7 | 63.6 | 41.8 | 12.5 |

*Distribution and Concentration.* The 15 animals that received 25 μc./kg. of polonium were used for this portion of the study. This dose proved to lie so close to the thirty day $LD_{50}$ that in several cases death occurred before the scheduled sacrifice time. As a result the series includes 2 animals each at one, three, ten, thirty, and thirty-eight days and only 1 animal at forty-five, fifty-one, sixty-six, and 120 days. This number, unfortunately, is small, but it does permit the establishment of orders of magnitude for the distribution and concentration of polonium in various organs.

The percentages of the retained dose found in the various organs are presented in Figure 5. This quantity was selected for illustration rather than the percentage of the injected dose in order to facilitate comparison between the organs and the body as a whole, and so that changes in distribution would not be masked by the decline in over-all retention. During the entire 120 day period relatively constant percentages of the retained polonium were found in the liver, skeleton,* and the mesenteric lymph node. The values for both the kidneys and the lungs decreased by a factor of 6, while for the spleen the value increased by a factor of 3. There was considerable variation in the polonium content of the ovaries sampled during the first ten days. The highest value was 1.3 per cent and the lowest 0.23 per cent; at 120 days no polonium could be detected in them.

The concentration of polonium in the various organs (μc./gm.) at from one to sixty-six

* Based on the approximation that a femur comprises one twentieth of the total skeleton.

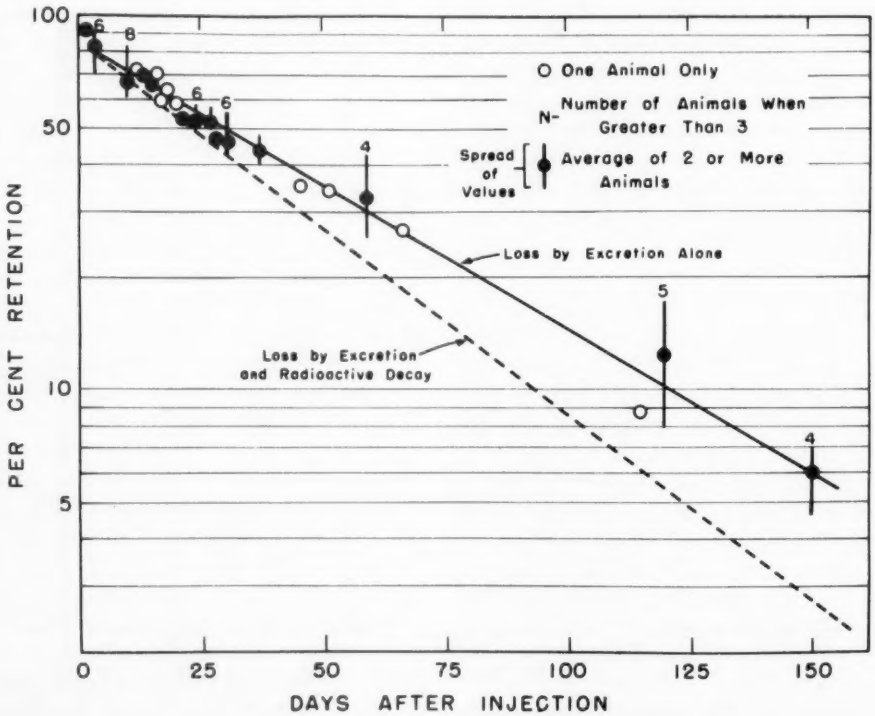


FIG. 4. Retention of polonium following intravenous administration.

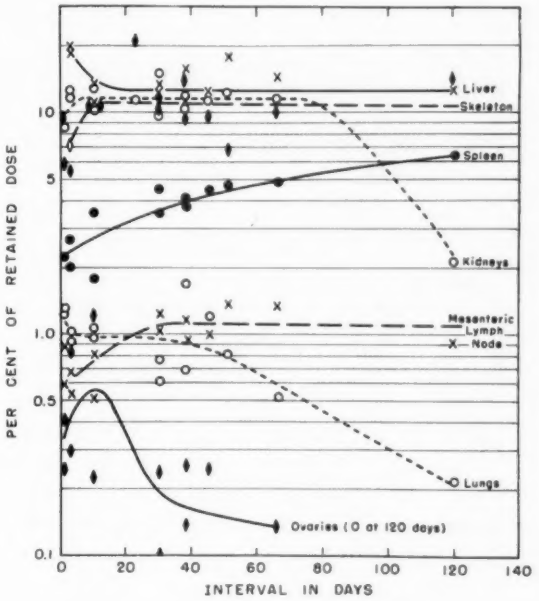


Fig. 5. Distribution of retained polonium: $\frac{\mu c. \text{ in organ} \times 100}{\mu c. \text{ in total animal}}$.

days expressed as the per cent of the injected dose in μc./gm. is illustrated in Figure 6. This method of presentation demonstrates the relative concentrations in the different organs and, in addition, it permits the calculation of the radiation dosage to an organ that will result from the administration of any amount of polonium. It is assumed that, since per cent retention proved to be independent of dose, distribution and concentration likewise are independent of dose. In fact, this situation was found to be the case for rats by Fink.[4] The curve that describes the total body concentration of polonium, or the concentration if deposition were uniform throughout the body, is actually the retention curve in terms of μc./gm. for this group of animals. At 120 days significant concentrations of polonium were found only in the spleen, the mesenteric lymph node, liver, and femur (Table III).

Since the weight of an organ is involved in the calculation of its polonium concentration, and since this weight may be influenced by irradiation from the contained polonium, attention should be given to organ weights. In Figure 7 these data are presented as the percentage of the weight found the day after injection. During a comparable 120 day period both the body weight and the spleen weight of con-

Table III

THE CONCENTRATION OF POLONIUM 120 DAYS AFTER INJECTION

$\frac{\mu c./gm. \text{ in tissue} \times 100}{\mu c./gm. \text{ injected}}$

| Organ | Per Cent |
|---|---|
| Spleen | 97 |
| Mesenteric lymph node | 25 |
| Liver | 9 |
| Femur | 9 |
| Kidneys | 4 |
| Total animal | 4 |
| Gastrocnemius muscle | 2 |
| Ovaries | 0 |
| Lungs | 0 |

trol CF#1 female mice have been found to increase 40 per cent. As was noted previously, the animals that were used for this portion of the study (the 25 μc./kg. group) failed to gain weight. However, the lungs and gastrocnemius muscle showed a 40 per cent gain, but all of this increase occurred after the sixty-sixth day. These organs were subjected to less irradiation than any of the others with the exception of the femur, which failed to grow even after the sixty-sixth day. The explanation for the lack of femur growth may lie in the fact that whereas

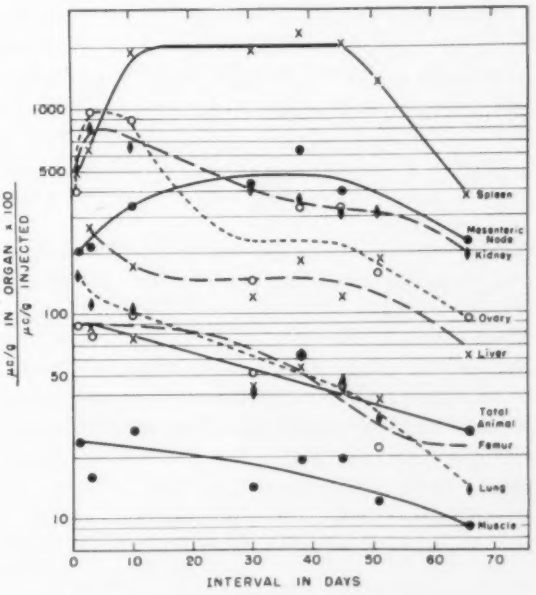


Fig. 6. Concentration of polonium: $\frac{\mu c./gm. \text{ in organ} \times 100}{\mu c./gm. \text{ injected}}$.

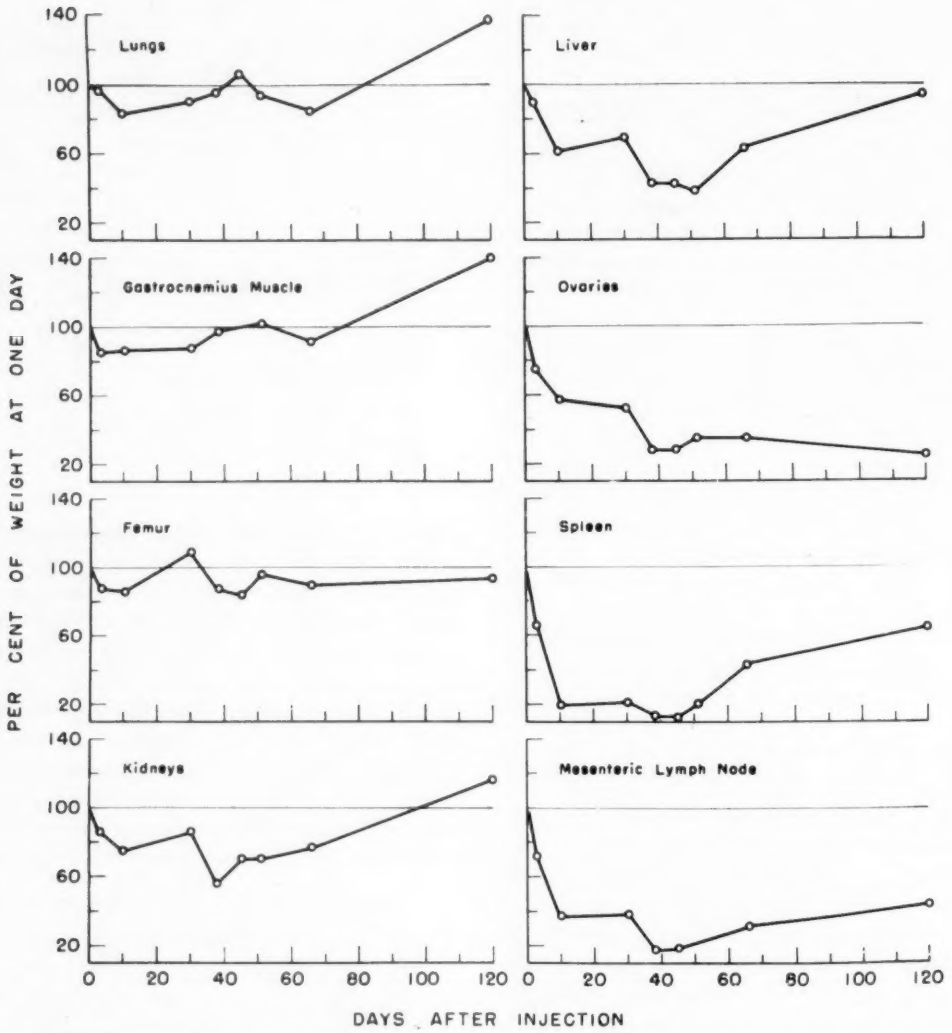


FIG. 7. Weight change of organs following intravenous administration of polonium 210. The weight on the day after injection establishes the base line of 100 per cent.

the concentration of polonium in the muscle and lungs was negligible at 120 days, that in the femur was still 9 per cent of the injected concentration (Table III). The kidneys received almost ten times as much irradiation as the femur during the first sixty-six days, and they responded with a significant decrease in weight. However, at 120 days the concentration of polonium in them was only 4 per cent of the injected concentration, and recovery is evidenced by the fact they weighed 17 per cent more than they had at one day. Although the liver received only about one-third as much irradiation as the kidneys on a weight basis during the first sixty-six days, it showed a greater loss of weight. In contrast to the kidneys, the liver did not exceed its initial weight at 120 days, and this again may be explained on the basis of the relative concentrations of polonium in these two organs at 120 days, *viz.*, 9 per cent for the liver and 4 per cent for the kidneys. From the sixty-sixth to the 120th day the concentration of polonium decreased in the kidneys by a factor of 50 and in the liver by a factor of 7. It appears that the ovaries were so severely damaged that, in spite of the fact that no polonium could be detected in them at 120 days, weight recovery did not occur. The spleen and the mesenteric lymph node showed the greatest proportional loss of weight and, with the exception of the ovaries, the least recovery. This is in accord with the fact that at

120 days their concentration of polonium was 97 per cent and 25 per cent, respectively, of the injected concentration.

## DISCUSSION

There appears to be little difference between the response of rats and that of mice to acutely lethal doses of polonium administered intravenously. A comparison of the data reported by Fink and his associates for the rat[4] and those reported here for the mouse shows only minor differences, which may well be the result of the small numbers of animals used rather than an actual species difference. For example, the percentage of the retained dose that was present in the rat spleen decreased from the tenth to the fiftieth day while in the mouse spleen it increased. Another discrepancy appears between the values for the concentration in the lung. The rat lung contained approximately two and one-half times as much polonium per gram of tissue as the average body tissue, whereas the concentration in the mouse lung remained very close to that of the body as a whole.

The liver, spleen, kidneys, and skeleton of the mouse contained between 30 and 60 per cent of the retained polonium during the first sixty-six days after injection. At 120 days 30 per cent of the retained material was present in the liver, spleen, and skeleton. No attempt was made to analyze separately the bone and bone marrow in this small animal, but Fink[4] has reported for the rat that on a weight basis the marrow contained five times as much polonium as the bone. Therefore, if "bone marrow" may be substituted for "skeleton," the distribution of polonium in the mouse is found to coincide closely with the principal locations of the reticuloendothelial cells. This distribution may result from the presence of polonium colloids. It was not possible to establish that polonium colloids did not exist in the injection solution. However, the fact that polonium forms colloidal aggregates in neutral solution strongly suggests that such aggregates appear rapidly upon injection. This hypothesis is substantiated by the work of Boyd,[1] who found polonium aggregates in the cardiac blood of the rat one and one-half minutes after intravenous administration. Within a few minutes appreciable amounts of polonium appeared in the liver, spleen, and bone marrow.

The concentration of polonium in particular organs and its uneven distribution within these organs complicates the calculation of radiation dosage. This situation is true for all radioisotopes that are not distributed uniformly. In spite of this difficulty there is, perhaps, some justification for translating the energy resulting from radioactive decay into a unit such as the roentgen equivalent physical (rep) so that the effects of one type of radiation may be compared with those of another for purposes of determining their relative biological effectiveness. If the assumption is made that 1 microcurie of polonium is evenly distributed within 1 gram of tissue, the dosage therein is equivalent to 294 rep/day. Calculation of the dosage to the various organs of those mice that received 25 μc./kg. reveals that, if the material had been evenly distributed within them, the spleen and the mesenteric lymph node received 170 and 48 rep/day, respectively, at the time that they had their highest polonium concentration. These values were reduced to 7 and 1.7 rep/day on the 120th day. Therefore, it is not surprising that these organs did not recover their pre-injection weight. Similarly, the ovaries were unable to recover after their initial maximum dose of 73 rep/day.

The uneven distribution of polonium among and within the organs indicates that at low levels the major pathological changes will be found in the lymphoid and myeloid tissues, renal cortex, ovaries, and perhaps in the liver. Casarette,[2] in his studies of rats that had received 10 or 20 μc./kg. one-half to 160 days previously, found changes in the peripheral blood, the lymphatic tissues, kidneys, and testes. Although polonium is not a bone seeking isotope, he found alterations in the zone of endochondral ossification in the femur,

primarily in the higher dosage group and at the later intervals. Therefore, it is not improbable that pathological changes will occur in the bones of those animals that receive above tolerance levels of polonium.

The ovary may prove to be the critical organ in determining the lowest injurious dose since it is one of the more radiosensitive organs and its concentration of polonium during the first ten days after injection was exceeded only by that of the spleen. Lorenz[14] found an increase in the incidence and a decrease in the latent period of ovarian tumors in $LAF_1$ mice that were subjected to gamma irradiation from radium at the rate of 0.11 r/day given in eight hours per day. The first tumor appeared when the total accumulated dose was approximately 90 r. The ovarian tumor incidence was the same as that following a single dose of 50 r roentgen radiation delivered in four and one-half hours. It can be calculated from the present study that at the lowest proposed dose for the long-term experiment (1/100 of the thirty day $LD_{50}$, or 0.4 μc./kg.) the ovaries will receive approximately 35 rep during the first sixty-six days, or an average of 0.5 rep/day. From the third through the tenth day after injection, the dose rate will be of the order of 1 rep/day.

## SUMMARY AND CONCLUSIONS

1. A reliable method for the quantitative determination of polonium 210 in animal tissues is presented.

2. The thirty day $LD_{50}$ of polonium given intravenously in hydrochloric acid solution to young adult CF#1 female mice lies between 30 and 40 μc./kg. The deleterious effects of 10 μc./kg. were manifest as early as two weeks after injection by the failure of the mice to grow.

3. The per cent retention of intravenously injected polonium was independent of dose level over the range studied (5 to 100 μc./kg.). Excretion alone reduced the body content to 71 per cent at ten days, 50 per cent at thirty days, 14.5 per cent at 100 days, and 6 per cent at 150 days. The biological half-period, including loss by radioactive decay, was thirty days.

4. During the first sixty-six days after the injection, the greatest portion of the retained polonium was located in the liver, kidneys, and skeleton. The major change at 120 days was the decrease in the polonium content of the kidneys.

5. During the first sixty-six days the concentration of polonium (μc./gm.) was greatest in the spleen, kidney, mesenteric lymph node, ovary, and liver. At 120 days the microcuries of polonium per gram of spleen were 97 per cent of the microcuries that had been injected per gram of animal. The value for the mesenteric lymph node was 25 per cent. At this time the concentrations in both the liver and the femur were 9 per cent of the initial concentration in the total animal.

6. The localization of polonium indicates the probable sites of pathological change after the administration of low doses of the isotope. It is suggested that the ovary may prove to be the critical organ in determining the lowest injurious dose.

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*Editor:* Lawrence Reynolds, 110 Professional Building, Detroit 1, Mich.

*Assistant Editor:* Ruth Bigelow, 110 Professional Building, Detroit 1, Mich.

*Fifty-fourth Annual Meeting:* Netherland Plaza Hotel, Cincinnati, Ohio, September 29–October 2, 1953.

### AMERICAN RADIUM SOCIETY

*President:* Edith H. Quimby, New York, N. Y.; *President-Elect:* John E. Wirth, Pasadena, Calif.; *1st Vice-President:* H. Dabney Kerr, Iowa City, Iowa; *2nd Vice-President:* Grant H. Beckstrand, Long Beach, Calif.; *Secretary:* Robert E. Fricke, Mayo Clinic, Rochester, Minn.; *Treasurer:* Douglas J. Roberts, 85 Jefferson St., Hartford 6, Conn.

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*Representatives on National Committee for Radiation Protection:* Edith H. Quimby, New York, N. Y., Theodore P. Eberhard, Philadelphia, Pa.

*Thirty-sixth Annual Meeting:* The Homestead, Hot Springs, Virginia, March 14, 15 and 16, 1954.

EDITORIAL

# SOME EARLY EXPERIENCES IN THERAPEUTIC RADIOLOGY; FORMATION OF THE AMERICAN RADIUM SOCIETY*

*By* JAMES T. CASE, M.D.
SANTA BARBARA, CALIFORNIA

AT A recent meeting of industrial surgeons an elderly doctor told me that I had found a kidney stone on him in 1903. I think his dates may have been slightly confused, for I believe I found my first case of kidney stone radiologically about 1906, possibly 1907, when I was working with Dr. W. F. Martin, urologist at the Battle Creek Sanitarium, who shortly turned over his x-ray room to me. As a medical student I had been playing with the x-rays as early as 1903, using an old static machine of giant size, probably 8 feet high, 10 feet long and 5 or 6 feet deep, capable of generating a very powerful spark. My first experiments were with cats, repeating the published investigations of W. B. Cannon on the motor physiology of the digestive tract. One day I was working with an open tube and hand fluoroscope, the cat being fastened down on a large plate-drying rack above the x-ray tube. Because I had failed to secure the cat's tail, its dreams were rudely interrupted by sudden contact of the tail with the high tension wire. The resulting "catsplosion" ruined my tube and interrupted my work until I could scrape up another thirty dollars for a new tube. But my pet cat still had all its nine lives and emerged from the accident almost unscathed, just slightly singed and still my friend.

In 1907, in addition to my routine work as surgical assistant, I found opportunity to continue radiological work with patients, spending whatever time was needed in the x-ray room, at first with Dr. Martin, then soon on my own.

My early experience in radiation therapy included mostly superficial skin lesions, the dose being measured by the Sabouraud-Noiré pastilles. For instruction in the use of these pastilles, I shall always be grateful to George E. Pfahler who in so many ways has been my inspiration and my mentor.

In the following years in our roentgen therapy we used the open lead-glass bowls with their inefficient protection, employing as protective materials at first lead, later lead-rubber fabrics; and, following the example of Dr. Pfahler, gradually going through the stage of leather, wet felt and aluminum filters. An inherent defect with the old gas tube was trouble in maintaining anything like constancy of voltage. The voltage was measured by the length of the spark gap between point and plate which the tube would back up. It was a crude method but the best available until later the sphere gaps were introduced.

In 1913 Dr. Coolidge brought out his hot cathode tube, and at that time he sent half a dozen of these tubes to Lewis Gregory Cole in New York to test for their roentgenographic behavior and he personally brought to me in Battle Creek a shipment to test their behavior in radiotherapy. He was soon satisfied that the rays

* Remarks made at the Annual Banquet at the Thirty-fifth Annual Meeting of the American Radium Society, St. Louis, Missouri, April 20–22, 1953.

emanating from the hot cathode tube were not therapeutically different from the rays generated in the old "conventional" gas tubes, and after that I continued to use the Coolidge tubes for therapy by employing as filter aluminum sheets 3 or 4 mm. in thickness.

In 1916 the German literature began to contain references to higher voltage and higher filtration for radiotherapy. This new work came especially from the University of Freiburg in Breisgau. Kroenig and Gauss in the gynecological clinic were developing new techniques in radium and roentgen therapy in pelvic diseases. I had ordered the construction of a transformer with 196 kv. capacity and with copper filters began the employment of the Coolidge tubes up to the limit of their endurance. Some of the original tubes would tolerate as much as 160 kv. for a month or two.

Participation of the United States in the First World War interrupted my practice but the higher voltage tests were resumed in 1919. The only tubes available for therapy were still the ordinary original Coolidge tubes. In 1921 I made another trip to Europe, spending time with Gauss (Kroenig had died), Friedrich, Holfelder, and various other Europeans interested in deep therapy, and I brought back meters from Germany and France for the measurement of dosage. Those interested will find a very fine account of all this early work in the 1936 Janeway Lecture by Curtis Burnam.[1]

On returning home I continued to use the highest voltage possible. Nowhere had I found more than 160 or 170 kv. in use, for the reason that the only available tubes would take no higher voltage. Coolidge was working on his first 200 kv. therapy tube—a large tube, nearly a yard long and with a much larger bulb than usual and therefore requiring a much larger lead-glass bowl than previously employed. We had not yet reached the stage of providing proper protection against the higher voltage tubes. In this, Leucutia of Detroit was one of the leaders. Our patients were protected by a heavy layer of leaded-rubber fabric supported from the floor by frames which could be moved over the parts of the body proximal and distal to the field under treatment. The field itself was arranged with sheet lead.

One day a gentleman brought his wife to me from Fort Wayne, Indiana, having been sent for the special x-ray treatment that the physicians there had heard I might be able to give. The patient had a recurrence of mammary carcinoma with positive biopsy of the supraclavicular glands. I explained that I knew of some advances in roentgen therapy and that I had an instrument which would give nearly 200,000 volt current if I could only get a tube which would stand that potential. I explained that Dr. Coolidge was working on such a tube and that I had seen it in operation in Schenectady, but that it was not yet on the market and would not be for nearly a year. The gentleman remarked that he would get Dr. Coolidge on the telephone and have one of the tubes for me "day after tomorrow." I tried to explain that it would be futile to try to get a tube, for it was not yet on sale, and that I could not ask for one; but he insisted that he would call Dr. Coolidge. When asked just who he was, he replied that he was the manager of the Fort Wayne branch of the General Electric Company. True to his promise, I had my tube within the forty-eight hours, and promptly burned out my 196 kv. transformer. The gentleman found me almost weeping over the loss of the special transformer, but after listening to my explanation, assured me that he would have another one of 300,000 volt capacity the "day after tomorrow," and sure enough, he did have one trucked up from Fort Wayne and we had it in operation on the third day. This first patient survived nearly eight years, all but the last few months in comfort and general good health, but finally succumbing to pleural malignancy. I went on with this deep roentgen therapy, receiving patients from far and near, and

[1] Burnam, C. F. Early experiences with radium; Janeway Memorial Lecture. AM. J. ROENTGENOL. & RAD. THERAPY, 1936, *36*, 437–452.

working days and evenings until the first 200,000 volt modified Snook type of transformer was put on the market. The first one was shipped to Battle Creek, and served long and well until replaced with a 400,000 volt instrument in 1937. It is obvious that I had the privilege of being the first to work on patients with 200 kv. roentgen therapy, thanks to the incident of having the wife of an important General Electric official as my patient.

At first we gave very large doses of deep roentgen therapy, so large in fact, and within so short a time, that most of the patients were forced to take to their beds for a week or so, and some of them were really prostrated. We often gave blood transfusions, and other supportive treatment. We early discovered that there was a definitely larger incidence of herpes zoster in patients who had had radiation therapy after operations for mammary carcinoma.

Meanwhile a supply of radium had gradually been acquired at the Battle Creek Sanitarium until we had 600 mg. This gave plenty of opportunity for early use of this new agent. I well recall the interest in radium therapy aroused at a meeting of the American College of Surgeons in Chicago when Howard A. Kelly, taking his place on the platform to speak, dramatically held up a small object between thumb and forefinger, and after a brief interval of impressive silence, announced "I hold in my hand one gram of radium!" He then proceeded to tell what one gram of radium would accomplish. Of course it was not actual radium in his fingers but a cubic centimeter of chalk, but it served to make his lecture highly impressive. The combination of radium with roentgen therapy had been utilized by us for several years, first with buccal, hypopharyngeal, esophageal and uterine carcinoma, and uterine fibroids. Prostatic cancer was treated with radium needles plus external roentgen therapy.

Now as to the beginnings of this Society: After a preliminary conference held during the American Medical Association meeting in Detroit in June, 1916, the American Radium Society was formally launched at the Rittenhouse Hotel in Philadelphia, October 26, 1916. A constitution was adopted by unanimous vote. W. H. Cameron, chairman of the committee, announced that there were nineteen active members and one associate member. The names are not included in the record, but based on a very careful review of the subsequent records, in my opinion, the names were as follows:

Robert Abbe, New York
W. H. B. Aikens, Toronto
C. B. Alliaume, Utica, New York
Joseph B. Bissell, New York
E. H. Boggs, Pittsburgh
W. R. Cameron, Pittsburgh
James T. Case, Battle Creek
Howard Fox, New York
S. C. Glidden, Danville, Illinois
T. C. Kennedy, Indianapolis, Indiana
J. M. Lee, Rochester, New York
Isaac Levin, New York
H. W. Longyear, Detroit
R. E. Loucks, Detroit
H. K. Pancoast, Philadelphia
D. T. Quigley, Omaha
M. M. Rosenthal, Fort Wayne, Indiana
Henry Schmitz, Chicago
F. E. Simpson, Chicago

and as associate member

C. H. Viol, Pittsburgh

Of these, the only survivors are D. T. Quigley and your speaker.

The first officers were Aikens, president; Boggs, vice-president; Pancoast, corresponding secretary; and Loucks, recording secretary and treasurer. Apparently the only scientific contribution was by C. H. Viol, a physicist, presumably on the physical aspects of radium therapy.

The *second* meeting took place in New York, June 4, 1917, with fifteen members present. Several of us were already in military service. A large number of new members were elected, including: Curtis Burnam, Baltimore; Walter B. Chase, New York; John G. Clark, Philadelphia; James A. Corscaden, New York; C. E. Field, New

York; H. H. Janeway of the Memorial Hospital, New York; Douglas Moriarta, Saratoga, New York; W. S. Newcomet, Philadelphia; E. C. Samuel, New Orleans; Albert Soiland, Los Angeles, and several others, twenty-five in all. Four papers were presented, including discussions of the physics of radium for the radiologist, radium in general surgical practice, methods of treating the lower urinary tract, histologic findings in tissues treated by radium (H. Schmitz), and case reports.

The *third* annual meeting occurred at the Palmer House, Chicago, June 10, 1918, with John M. Lee presiding, with only sixteen members present, military duties accounting for the absence of a number (including myself). Robert Abbe of New York was elevated to honorary membership, but he said he preferred to remain active, so the motion electing him was amended to read "active honorary member." The balance in the Society's funds was $114.80. This meeting marked the first participation of James Ewing in the program of the Society, an association that was to prove so valuable in the ensuing years. New members elected included Leda Stacy of the Mayo Clinic; W. L. Clark, Philadelphia, and Gioacchino Failla, of the Memorial Hospital, New York. Papers were listed on the use of radium in gynecology (T. J. Watkins and Leda Stacy) and others on radiation physics and radium in general practice.

The *fourth* meeting occurred in Atlantic City, June 9, 1919, under the chairmanship of Henry Schmitz, Chicago (in the absence of the president, F. E. Simpson, who was ill). Seventeen members and twenty-eight guests were present. The treasurer closed the year with $130.70. This scientific meeting included papers by George E. Pfahler, on the combination of radium, x-rays and electrocoagulation with surgery in the treatment of malignant disease, a paper by Albert Soiland on the comparative action of radium and x-rays, and a paper on the treatment of arthritis with radium (apparently by oral administration). Fifty members and guests were present. New members included Gerber, Kirkendahl, Pfahler, Quick, Skinner, Rollin Stevens, and others. This was the first year, I believe, in which qualifications for membership were formalized. Applications were required to state data regarding graduation, amount of radium in possession, and to include a report of twenty-five cases treated. A research committee was appointed for the purpose of standardizing records and reporting radium treatments. Janeway reported on deeply implanted radium emanation tubes.

The *fifth* annual meeting took place in New Orleans, April 26, 1920, with Henry K. Pancoast presiding. The scientific papers had relation chiefly to gynecologic applications of radium, including a report by Stacy on 600 cases of menorrhagia and uterine myomas. C. Jeff Miller of New Orleans, Skinner and Schmitz also took part in this gynecologic symposium. Other contributions included angiomas treated by radium, and Janeway had another paper on the use of emanations. G. E. Pfahler talked on cancer of the breast. J. M. Martin of Dallas presented a movie of his work with early and late carcinoma treated with radiotherapy, for which he was given a special vote of thanks.

At the *sixth* annual meeting in Boston, 1921, under the presidency of Henry Schmitz, the guests of honor were Elis Berven of Stockholm and W. D. Coolidge. The annual dues were increased to $12.00 to include subscription to the American Journal of Roentgenology, which had been selected as the official organ of our Society, and the name was changed, beginning with the January, 1923, issue, by the addition of the words "and Radium Therapy." The death of Henry H. Janeway, head of the radium department of the Memorial Hospital, New York, dampened the spirits at this meeting. Janeway was especially known as the first in America to use radium emanation buried in tumor growths, for his early work in uterine carcinoma, and for his efforts to standardize

dosage and accurate technique of application of radium.

The *seventh* meeting, 1922, under the presidency of George E. Pfahler was noted for the effort made to secure a ruling by the Internal Revenue Department, asking that the purchase price of radium for therapeutic purposes be declared deductible as expense, provided that in the event of sale of the radium the amount received be recorded as income. You all know that this effort was in vain. William Duane, W. D. Coolidge, and Claude Regaud were elected honorary members at this meeting.

The *ninth* annual meeting, 1924, was held in Chicago, under the presidency of your speaker. Four distinguished scientists were elected honorary members, including James Ewing, Gösta Forssell, Ernest Rutherford, and A. E. Hayward Pinch. Robert Abbe, Madame Curie, Howard A. Kelly and Francis H. Williams had already been made honorary members. It was a matter of particular pride that I had been able to arrange for the presence of Dr. Claude Regaud, of the Curie Institute of Paris. His address was the great event of the meeting.

On this visit Prof. Regaud had been breakfasted and lunched and dined by various medical organizations, radiological and otherwise, in New York, Philadelphia, Washington, and other centers, including Chicago, so that he had had very little time for himself. After returning home he wrote me a letter, recognizing my good offices in arranging his American visit and thanking me profusely for the "wonderful but terrible American hospitality," with which he had been entertained, and inviting our members to visit the Radium Institute of the University of Paris.

These remarks, perhaps much too personal, must close here. I am sure I will be forgiven for not following further the details of progress of this Society. It has been a real treat to have the old records made available to me by our worthy secretary, Dr. Wirth. I have read them through from the first meeting to within recent years. It is a valuable collection of documents, albeit some of them are much too brief. While mourning the passing of so many of my friends, it has brought a thrill of pride to realize that I have had the privilege of having been associated with them, pride in their accomplishments in the advancement and establishment of radium therapy in its present position as one of the main dependencies in the management of malignant disease and of many allied affections. I wish also once more to express my thanks to you for your consideration in giving me this place of prominence at the banquet table this evening and for having listened to me so patiently.

2315 Bath St.
Santa Barbara, California

# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

## MEETINGS OF ROENTGEN SOCIETIES*

### UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
*Secretary*, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 29–Oct. 2, 1953.

AMERICAN RADIUM SOCIETY
*Secretary*, Dr. R. E. Fricke, Mayo Clinic, Rochester, Minn. Annual meeting: The Homestead, Hot Springs, Virginia, March 14–16, 1954.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
*Secretary*, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: Palmer House, Chicago, Ill. Dec. 13–18, 1953.

AMERICAN COLLEGE OF RADIOLOGY
*Executive Secretary*, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
*Secretary*, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: 1954, to be announced.

FIFTH INTER-AMERICAN CONGRESS OF RADIOLOGY
*General Secretary*, Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa. Meeting at Shoreham Hotel, Washington, D. C., April 24–30, 1955.

ALABAMA RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

ARIZONA RADIOLOGICAL SOCIETY
*Secretary*, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS RADIOLOGICAL SOCIETY
*Secretary*, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

ATLANTA RADIOLOGICAL SOCIETY
*Secretary*, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

BROOKLYN ROENTGEN RAY SOCIETY
*Secretary*, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

BUFFALO RADIOLOGICAL SOCIETY
*Secretary*, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
*Secretary*, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

CENTRAL OHIO RADIOLOGICAL SOCIETY
*Secretary*, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

CHICAGO ROENTGEN SOCIETY
*Secretary*, Dr. Elbert K. Lewis, 6337 S. Harvard Ave., Chicago, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

CLEVELAND RADIOLOGICAL SOCIETY
*Secretary*, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

COLORADO RADIOLOGICAL SOCIETY
*President*, Dr. W. P. Stampfli, St. Luke's Hospital, Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
*Secretary*, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB
*Secretary*, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
*Secretary*, Dr. E. F. Lang, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

EAST BAY ROENTGEN SOCIETY
*Secretary*, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

FLORIDA RADIOLOGICAL SOCIETY
*Secretary*, Dr. A. Judson Graves, 2002 Park St., Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
*Secretary*, Dr. Robert M. Tankesley, 218 Doctors Bldg., Atlanta, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

GREATER MIAMI RADIOLOGICAL SOCIETY
*Secretary*, Dr. E. H. Bryson, 273 Alhambra Circle, Coral Gables, Fla. Meets third Wednesday of each month at Veterans Administration Building.

HOUSTON RADIOLOGICAL SOCIETY
*Secretary*, Dr. Harry Fishbein, 324 Medical Arts Bldg., Houston 2, Texas. Meets fourth Monday each month at Hermann Hospital.

IDAHO STATE RADIOLOGICAL SOCIETY
*Secretary*, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

ILLINOIS RADIOLOGICAL SOCIETY
*Secretary*, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
*Secretary*, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

IOWA RADIOLOGICAL SOCIETY
*Secretary*, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

KANSAS RADIOLOGICAL SOCIETY
*Secretary*, Dr. Willis L. Beeler, M.D., 700 Kansas Ave., Topeka, Kansas. Meets in spring with State Medical Society, and in winter on call.

KENTUCKY RADIOLOGICAL SOCIETY
*Secretary*, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

KINGS COUNTY RADIOLOGICAL SOCIETY
*Secretary*, Dr. Marcus Wiener, 1430 48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
*Secretary*, Dr. George Jacobson, 1200 N. State St., Los Angeles 33, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Louisiana Radiological Society
*Secretary*, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Maine Radiological Society
*Secretary*, Dr. Hugh Allan Smith, Eastern Maine General Hospital, Bangor, Maine. Meets in early spring, June and fall.

Maryland Radiological Society
*Secretary-Treasurer*, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Maryland.

Miami Valley Radiological Society
*Secretary*, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

Mid-Hudson Radiological Society
*Secretary*, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

Milwaukee Roentgen Ray Society
*Secretary*, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
*Secretary*, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

Mississippi Radiological Society
*Secretary*, Dr. John W. Evans, 117 N. President St., Jackson, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

Montana Radiological Society
*Secretary*, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Will meet at least once a year.

Nassau Radiological Society
*Secretary*, Dr. Frank Huber, Hempstead, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

Nebraska Radiological Society
*Secretary*, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

New England Roentgen Ray Society
*Secretary*, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

New Hampshire Roentgen Ray Society
*Secretary*, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
*Secretary*, Dr. J. R. Freid, 1049 Park Ave., New York 28, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
*Secretary*, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

North Dakota Radiological Society
*Secretary*, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

Northeastern New York Radiological Society
*Secretary*, Dr. John F. Roach, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April. Annual meeting will be held in May or June, 1953.

Northern California Radiological Society
*Secretary*, Dr. H. B. Stewart, 2920 Capitol Ave., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

Ohio State Radiological Society
*Secretary*, Dr. M. M. Thompson, 316 Michigan St., Toledo, Ohio.

Oklahoma State Radiological Society
*Secretary*, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

Oregon Radiological Society
*Secretary*, Dr. J. Richard Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

Orleans Parish Radiological Society
*Secretary*, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
*Secretary*, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
*Secretary*, Dr. J. M. Converse 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
*Secretary*, Dr. H. M. Stauffer, Temple University Hospital, Philadelphia 40, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
*Secretary*, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets 6:00 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Radiological Section, Baltimore Medical Society
*Secretary*, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

Radiological Section, Connecticut Medical Society
*Secretary*, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

Radiological Section, Medical Society of the District of Columbia
*Secretary*, Dr. A. C. Wyman, 5445—28th St., N.W., Washington, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Radiological Section, Southern Medical Association
*Secretary*, Dr Roy G. Giles, Temple, Texas.

Radiological Society of Greater Cincinnati
*Secretary*, Dr. Chapin Hawley, 927 Carew Tower, Cincinnati 2, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

Radiological Society of Hawaii
*Secretary*, Dr. P. S. Arthur, Young Hotel Bldg., Honolulu 13, T. H. Meets third Friday of each month at a place designated by the Secretary.

Radiological Society of Kansas City
*Secretary*, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of New Jersey
*Secretary*, Dr. Salomon Silvera, 921 Bergen Ave., Jersey City, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

Richmond County Radiological Society
*Secretary*, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga.

Rochester Roentgen Ray Society, Rochester, N. Y.
*Secretary*, Dr. A. Gordon Ide, 277 Alexander St., Rochester 7, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

Rocky Mountain Radiological Society
*Secretary*, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Next annual meeting, Shirley-Savoy Hotel, Denver, Colo., August 20, 21 and 22, 1953.

St. Louis Society of Radiologists
*Secretary*, Dr. Francis O. Trotter, Jr., 634 N. Grand Blvd., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August and September.

San Antonio-Military Radiological Society
*Secretary*, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets Brook Army Medical Center Officers Mess first Monday of each month.

San Diego Radiological Society
*Secretary*, Dr. C. W. Bruner, 2456 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
*Secretary*, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
*Secretary*, Dr. Calvin L. Stewart, 2330 First Ave., San Diego 1, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
*Secretary*, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
*Secretary*, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH BAY RADIOLOGICAL SOCIETY
*Secretary*, Dr. W. H. Graham, 634 East Santa Clara St., San Jose 12, Calif. Meets second Wednesday each month.

SOUTH CAROLINA RADIOLOGICAL SOCIETY
*Secretary*, Dr. William A. Klauber, Self Memorial Hospital, Greenwood, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

TENNESSEE RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. M. Frère, Newell Hospital, Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
*Secretary*, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort worth 4, Texas. Next meeting, Dallas, Texas, Jan. 29 and 30, 1954.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
*Secretary*, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

UTAH STATE RADIOLOGICAL SOCIETY
*Secretary*, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

VIRGINIA RADIOLOGICAL SOCIETY
*Secretary*, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
*Secretary*, Dr. John N. Burkey, 555 Medical-Dental Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May.

WESTCHESTER RADIOLOGICAL SOCIETY
*Secretary*, Dr. Clifford C. Baker, Harwood Bldg., Scarsdale, N. Y. Meets on third Tuesdays of January and October and on two other dates.

WISCONSIN RADIOLOGICAL SOCIETY
*Secretary*, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-RAY STUDY CLUB OF SAN FRANCISCO
*Secretary*, Dr. Wm. W. Saunders, Veterans Administration Hospital, San Francisco 21, Calif. Meets monthly, third Thursday, at 7:45 P.M., Lane Hall, Stanford University Hospital.

### CUBA, MEXICO, PUERTO RICO AND CENTRAL AMERICA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
*President*, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

SOCIEDAD MEXICANA DE RADIOLOGIA Y FISIOTERAPIA
*General Secretary*, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA
*Secretary*, Dr. Rafael A. Blanes, Ave. Ponce de Leon 1175, Santurce, P. R.

SOCIEDAD RADIOLÓGICA PANAMEÑA
*Secretary*, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

### BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

FACULTY OF RADIOLOGISTS
*Honorary Secretary*, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

CANADIAN ASSOCIATION OF RADIOLOGISTS
*Honorary Secretary-Treasurer*, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
*Secretary*, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES
*Secretary*, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

COLLEGE OF RADIOLOGISTS (AUSTRALIA AND NEW ZEALAND)
*Honorary Secretary*, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

### SOUTH AMERICA

ASOCIACION ARGENTINA DE RADIOLOGIA
*Secretary*, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, JUNTA CENTRAL, BUENOS AIRES
*Secretary*, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL LITORAL, SEDE, ROSARIO
*President*, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL SUR, SEDE, LA PLATA
*President*, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL CENTRO SEDE, CORDOBA
*President*, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL NORTE, SEDE, TUCUMAN
*President*, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DE CUYO SEDE, MENDOZA.
*President*, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

SOCIEDADE BRASILEIRA DE RADIOLOGIA MEDICA
*Secretary*, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
*Secretary*, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD COLOMBIANA DE RADIOLOGIA
*Secretary*, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6º piso, Bogota, Colombia. Meets last Thursday of each month.

SOCIEDAD PERUANA DE RADIOLOGIA
*Secretary*, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January,

February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
*Secretary*, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

### Continental Europe

Société Belge de Radiologie
*General Secretary*, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Société Française d'Electro-Radiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord
*Secretary-General*, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX°, France.

Ceskoslovensk společnost pro rëntgenologii a Radiologii v Praze
*Secretary*, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
*Secretary*, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
*Secretary*, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

Wrocław Section Polish Society of Radiology
*Secretary*, Dr. R. Marciniak, Akad. Medyczna Wrocław, 68 Curie-Skłodowska St., Wrocław, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wrocław.

Societatea Romana de Radiologie si Electrologie
*Secretary*, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
*Secretaries*, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
*Secretary*, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
*Secretary*, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Deutsche Roentgen-Gesellschaft
*Secretary*, Dr. Peter Kröker, (22a) Essen-Helsingen, Westpreussenstrasse 21. Meets annually in different towns.

Societa Italiana di Radiologia Medica
*Secretary*, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

### India

Indian Radiological Association
*Secretary*, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

## THE PROFESSIONAL BUREAU

The Professional Bureau, a placement service for residents in radiology, sponsored by the American College of Radiology, invites all men in their last year of residency to register with the Bureau six to eight months prior to the termination of their service. Upon registration, they will receive a listing of all positions, assistantships, practices for sale, and locations for radiologists, on file at that time. In addition, their names will be put on the Bureau mailing list so that they will receive announcements of all subsequent requests for radiologists. *No charge will be made for any services rendered to either the registrant or the employer.* All senior residents who are eligible for the examinations by the American Board of Radiology are also eligible for registration with the bureau. A Biographical Data blank for the purpose of registering may be obtained by wiring or writing to Dr. S. W. Donaldson, Director, Professional Bureau, 326 North Ingalls St., Ann Arbor, Michigan.

## CONTINUATION COURSE IN RADIATION THERAPY FOR SPECIALISTS

The University of Minnesota announces a Continuation Course in Radiation Therapy for Specialists which will be held at the Center for Continuation Study on the University campus from October 26 to 31, 1953. Principles and clinical applications of all forms of radiation therapy will be discussed. The guest faculty will include Dr. Robert McWhirter, Professor, Department of Radiotherapy, Royal Infirmary, Edinburgh; Dr. Raymond Zirkle, Institute of Radiobiology and Biophysics, University of Chicago; Dr. Edith H. Quimby, Department of Radiology, Columbia University, New York; and Dr. Lauren V. Ackerman, Professor of Surgical Pathology and Pathology, Washington University School of Medicine, St. Louis, Missouri. The course will be presented under the direction of Dr. Leo G. Rigler, Professor and Head, Department of Radiology, and Dr. K. W. Stenstrom, Director of Radiation Therapy. Members of the faculty of the University of Minnesota Medical School and the Mayo Foundation will complete the faculty for the course.

## REORGANIZATION OF TECHNICAL STAFF OF ISOTOPES DIVISION

The Isotopes Division, United States Atomic Energy Commission, Oak Ridge, Tennessee, announces a reorganization of its technical staff. The Isotopes Division is the Atomic Energy Commission unit responsible for the national and international distribution of stable and radioactive isotopes. Under the new set-up, the Division will consist of three major branches.

The Allocations Branch will review and act upon all applications for isotopic materials; the Radiological Safety Branch will assist radioisotope users in matters of health protection, and the Technical Developments Branch will be responsible for preparing and disseminating information on isotope utilization and for outlining and encouraging training in isotope techniques.

Key personnel of the Division are: Paul C. Aebersold, Director; Charles E. Crompton, Assistant Director; Stephen P. Cobb, Jr. Technical Assistant to the Director; James R. Mason, Chief, Allocations Branch; G. W. Morgan, Chief, Radiological Safety Branch; Edwin A. Wiggin, Chief, Technical Developments Branch.

## CLINICAL FELLOWSHIPS IN RADIATION THERAPY OF THE AMERICAN CANCER SOCIETY

American Cancer Society Clinical Fellowships in Radiation Therapy are offered to properly qualified graduates in medicine who have already received thorough basic training in the principles and practice of radiation therapy, and who desire to spend additional periods of training in that specialty at certain clinics in the United Kingdom, the Scandinavian countries and France.

Fellowships are available to (1) citizens of the United States, (2) who are graduates of recognized Medical Schools in the United States, (3) who have previously received training in therapeutic radiology acceptable to the American Board of Radiology as credit toward certification, and (4) who are under forty years of age. In the selection of applicants, priority will be given to physicians who (1) are already certified by the American Board of Radiology, (2) who have completed the required training in preparation for Board examinations but who have not yet taken the examinations, and (3) those who, while intending to complete Board requirements and take the examinations, are still in the training period.

The annual stipend for Fellows in Radiation Therapy is $4,500.00 per year, including travel.

When such a Fellowship is awarded, an initial travel fund of $900.00 will be paid to the recipient. The remainder of the stipend will be paid in advance in monthly installments of $300.00, beginning with the Fellowship period.

The Fellowship period shall be one year, although in exceptional circumstances, and when not competing with new applications, renewal for one year or less will be considered.

All arrangements for affiliation with foreign institutions in which the Fellowship year is to be passed, shall be made by the applicant or his preceptor directly with the appropriate officials in those institutions, and the American Cancer Society will assume no responsibility therefor.

Acceptance of Fellows for training in foreign institutions must precede submission of applications to the American Cancer Society.

Fellows shall render to the American Cancer Society such reports of progress or accomplishments as shall be requested.

Applications for fellowships may be secured by writing Dr. Brewster S. Miller, Director Professional Education Section, American Cancer Society, 47 Beaver St., New York 4, New York.

## UROLOGY AWARD

The American Urological Association offers an annual award of $1000.00 (first prize of $500.00, second prize $300.00 and third prize $200.00) for essays on the result of some clinical or laboratory research in Urology. Competition shall be limited to urologists who have been in such specific practice for not more than ten years, and to men in training to become urologists.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Waldorf-Astoria, New York City, May 31–June 3, 1954.

For full particulars write the Executive Secretary, William P. Didusch, 1120 North Charles Street, Baltimore 1, Maryland. Essays must be in his hands before February 1, 1954.

Miley B. Wesson, *Chairman*
*Committee on Scientific Research*

## ANNOUNCEMENT OF VAN METER PRIZE AWARD

The American Goiter Association again offers the Van Meter Prize Award of Three Hundred Dollars and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the Association which will be held in Boston, Massachusetts, April 29, 30 and May 1, 1954, providing essays of sufficient merit are presented in competition.

The competing essays may cover either clinical or research investigations; should not exceed three thousand words in length; must be presented in English, and a typewritten double spaced copy in duplicate sent to the Corresponding Secretary, Dr. John C. McClintock, 149½ Washington Avenue, Albany 10, New York, not later than January 15, 1954. The committee, who will review the manuscripts, is composed of men well qualified to judge the merits of the competing essays.

A place will be reserved on the program of the annual meeting for the presentation of the Prize Award Essay by the author, if it is possible for him to attend. The essay will be published in the annual proceedings of the Association.

John C. McClintock, M.D.
*Corresponding Secretary*

## SECOND INTERNATIONAL CONGRESS OF CARDIOLOGY

The Second International Congress of Cardiology will be held in Washington, D. C., September 12–15, 1954. It will be immediately followed by the Annual Scientific Sessions of the American Heart Association, September 16–18, 1954. The opening session will be held in the auditorium of Constitution Hall at 10:30 A.M. on Sunday, September 12, 1954, with addresses of welcome. A reception will be given at the Mayflower Hotel at 5:00 P.M. on the same day for all members of the Congress and their families. A banquet will be held September 15, 1954, at 7:30 P.M.

The Scientific Sessions lasting for three days will include formal papers, panel discussions, clinical pathological conferences and visits to important medical centers in Washington and Bethesda. The program will be printed in French, Spanish and English. Immediate translation of some of the papers and discussions will be made in three languages.

A series of Post-Congress visits and conferences to at least twenty of the leading cardiac clinics in different parts of the United States and Canada has been arranged by special committees of local heart associations in the various cities.

Further information may be obtained from the Secretary-General, Dr. L. W. Gorham, 44 East 23rd St., New York 10, New York.

### ARIZONA RADIOLOGICAL SOCIETY

At the last annual meeting of the Arizona Radiological Society, the following officers were elected for the coming year: *President*, Dr. Bruce M. Crow, Mesa, Arizona; *Vice President*, Dr. Walter T. Hileman, Tucson, Arizona; *Secretary-Treasurer*, Dr. R. Lee Foster, 507 Professional Building, Phoenix, Arizona.

### ATLANTA RADIOLOGICAL SOCIETY

At a recent meeting of the Atlanta Radiological Society the following officers were elected for the coming year: *President*, Dr. Calvin B. Stewart, Atlanta, Georgia; *Vice President*, Dr. Ted Leigh, Emory University, Georgia; *Secretary*, Dr. Albert A. Rayle, Jr., Atlanta, Georgia.

### DETROIT ROENTGEN RAY AND RADIUM SOCIETY

At a recent annual meeting the following officers were elected by the Detroit Roentgen Ray and Radium Society: *President*, Dr. H. C. Jones, Grand Rapids, Michigan; *Vice President*, Dr. James C. Cook, Detroit, Michigan; *Secretary-Treasurer*, Dr. E. F. Lang, Harper Hospital, Detroit 1, Michigan.

### GEORGIA RADIOLOGICAL SOCIETY

The newly elected officers of the Georgia Radiological Society are: *President*, Dr. Stephen W. Brown, Augusta, Georgia; *Vice President*, Dr. John M. Barner, Athens, Georgia; *Secretary-Treasurer*, Dr. Robert M. Tankesley, 218 Doctors Building, Atlanta, Georgia. This meeting was held in conjunction with the State Medical Association. Dr. Robert D. Moreton of Ft. Worth, Texas, was guest speaker.

### MARYLAND RADIOLOGICAL SOCIETY

At the initial meeting of the Maryland Radiological Society, the following officers were elected for the coming year: *Chairman*, Dr. Richard B. Hanchett, Baltimore, Maryland; *Vice-Chairman*, Dr. E. T. Campbell, Hagerstown, Maryland; *Secretary-Treasurer*, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Maryland.

### NASSAU RADIOLOGICAL SOCIETY

At the June, 1953, meeting of the Nassau Radiological Society the following officers were installed for the coming year: *President*, Dr. James Barnett, Hicksville, New York; *Vice President*, Dr. Samuel Herstone, Bay Shore, New York; *Secretary*, Dr. Frank Huber, Hempstead, New York; *Treasurer*, Dr. Benjamin Stein, Hempstead, New York.

### OHIO STATE RADIOLOGICAL SOCIETY

At the annual meeting of the Ohio State Radiological Society held at Dayton, Ohio, May 23 and 24, 1953, the following officers were elected: *President*, Dr. Austin J. Brogan, Dayton, Ohio; *Vice President*, Dr. Willis S. Peck, Toledo, Ohio; *Secretary-Treasurer*, Dr. M. M. Thompson, Jr., 316 Michigan St., Toledo, Ohio.

### PITTSBURGH ROENTGEN SOCIETY

At the meeting of the Pittsburgh Roentgen Society held on June 10, 1953 the following officers were elected: *President*, Dr. Edwin J. Euphrat; *Vice President*, Dr. Peter Feltwell; *Secretary*, Dr. Donald H. Rice, 4800 Friendship Ave., Pittsburgh 24, Pennsylvania; *Treasurer*, Dr. Newton Hornick.

### RADIOLOGICAL SECTION OF THE BALTIMORE MEDICAL SOCIETY

At a recent meeting of the Radiological Section of the Baltimore Medical Society, the following officers were elected for the coming year: *Chairman*, Dr. David N. Gould, Baltimore, Maryland; *Secretary-Treasurer*, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Maryland.

### SECTION ON RADIOLOGY OF THE MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA

At the last meeting of the Section on Radiology of the Medical Society of the District of Columbia the following were elected to serve from May, 1953, to May, 1954: *President*, Dr. Alfred A. J. Den; *Vice President*, Dr. David H. Rodenfeld; *Secretary*, Dr. Alvin C. Wyman, all of Washington, D. C.

### RADIOLOGICAL SOCIETY OF HAWAII

At the last meeting of the Radiological Society of Hawaii on June 19, 1953, the following officers were elected for the coming year: *Presi-*

*dent*, Dr. Tetsui Watanabe, Honolulu; *Vice President*, Dr. Peter Washko, Honolulu; *Secretary-Treasurer*, Dr. Philip S. Arthur, Young Hotel Bldg., Honolulu 13, Hawaii.

Meetings are held on the third Friday of each month at a place to be designated by the Secretary.

## WISCONSIN RADIOLOGICAL SOCIETY

The annual meeting of the Wisconsin Radiological Society was held on May 23, 1953, at Beloit, Wisconsin. Dr. S. H. Squire of Chicago, the guest speaker, discussed "Cerebral Angiography." Other papers were presented by the members. At the business meeting, the following officers were elected: *President-elect*, Dr. Irving I. Cowan, Milwaukee, Wisconsin; *President*, Dr. Ralph L. Troup, Green Bay, Wisconsin; *Secretary-Treasurer*, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wisconsin.

# ABSTRACTS OF RADIOLOGICAL LITERATURE

*Department Editor:* T. LEUCUTIA, M.D., Harper Hospital, Detroit 1, Michigan

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## ROENTGEN DIAGNOSIS

### Head

Haar, H., and Tiwisina, Th. Die angiographische Differentialdiagnose des parasagittalen und des Falx-Meningioms. (The differential diagnosis of parasagittal and falx meningiomas by angiography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Dec., 1952, *77*, 653–661.

I. Meningiomas in the anterior third:

A. Parasagittal meningiomas: In the posteroanterior projection, the anterior cerebral vessels are displaced to the opposite side. The ascending branch of the anterior cerebral artery may form an angle of 120 degrees with the callosomarginal artery. The apex of the angle is at the knee of the corpus callosum. Tumors of the frontal region form a greater angle or curve than those of the frontoparietal area. The carotid syphon is stretched and flattened; the sylvian group is compressed. The midline vessels are pressed against the falx, which is bowed or obliquely displaced to the contralateral side (positive falx sign).

The lateral angiogram shows a posterior displacement of the cerebral vessels, compression of the carotid syphon, and downward displacement of the insular branch of the middle cerebral artery.

B. Falx meningiomas: In the posteroanterior projection, the ascending branch of the anterior cerebral artery is displaced to the opposite side and forms a semicircle with the insular branch of the middle cerebral artery and the carotid syphon. The falx sign is negative.

In the lateral view, there is a downward displacement of the anterior cerebral and the pericallosal arteries. The anterior group is crowded together. The phlebogram shows an occipitobasal displacement of the vein of Galen in the roof of the third ventricle.

II. Meningiomas in the middle third:

A. Parasagittal meningiomas are characterized by the same signs in the posteroanterior view as those in the anterior third.

B. Falx meningiomas produce a parallel displacement of the ascending branch of the anterior cerebral artery to the opposite side so that the pericallosal artery branches off at a right angle. The falx sign is negative. The sylvian group is not fanned out.

In the lateral projection, the pericallosal artery presents a basal convexity not seen in parasagittal meningiomas.

III. Meningiomas in the posterior third (better visualized by vertebral angiography):

A. Parasagittal meningiomas: In the posteroanterior projection there is compression of the sylvian group in a craniocaudal direction.

The lateral angiogram shows a basal displacement of the angular artery.

B. Falx meningiomas: The angiogram in the posteroanterior projection shows a parallel displacement of the anterior cerebral vessels to the contralateral side. The falx sign is positive.

The lateral angiogram shows a spreading of the sylvian group. The branches of the middle cerebral artery are stretched and convex upwards.—*Joseph Zausner, M.D.*

Polani, P. E. Encephalo-trigeminal angiomatosis (Sturge-Weber syndrome) treated by removal of the affected cerebral hemisphere. *Proc. Roy. Soc. Med.*, Dec., 1952, *45*, 860–862.

Two cases of Sturge-Weber syndrome treated by cerebral hemispherectomy are presented.

Case I. Six year old female with a history of right-sided fits since the age of three months. Sitting, talking and walking were delayed with development of moderately severe temper tantrums and management problems developing in the fifth year. A large left trigeminal nevus was seen at birth.

Examination showed right-sided hemiplegia with slight spasticity and right homonymous hemianopsia. Mental development was markedly retarded.

Electroencephalogram suggested more or less complete absence of function of the left cerebral hemisphere.

Roentgenograms of the skull showed the left half of the cranial cavity to be smaller than the right. Throughout the left hemisphere there wsa a widespread "tramlines" pattern of calcified streaks. Pneumoencephalography disclosed a markedly shrunken left cerebral hemisphere.

Left lateral craniotomy with left cerebral hemispherectomy was performed with preservation of the caudate nucleus and thalamus. Following the operation, the child's disposition improved, and she talked more and with improved articulation.

Case II. Four year old male child with similar history and physical findings. Hemispherectomy resulted in cessation of fits and general improvement comparable to Case I.

Few cases have been reported in the literature, and their follow-ups are necessarily short.

Presently it is considered that when severe infantile hemiplegia is present, hemispherectomy should be undertaken if (1) the fits cannot be controlled with adequate medical treatment, (2) there is a severe behavior disturbance which interferes with socialization of the patient, and (3) there is intellectual impairment with deterioration.—*Donald R. Bernhardt, M.D.*

MARTIN, FRANKLIN, JR., and LEMMEN, LLOYD J. Calcification in intracranial neoplasms. *Am. J. Path.*, Nov.–Dec., 1952, *28*, 1107–1131.

The authors' study consisted of histologically verified intracranial tumors of all types treated in the Department of Surgery at the University of Michigan during the period of 1930–1950.

Their classification generally follows that of Bailey and Cushing, except that spongioblastoma polare has been grouped with the astroblastomas. For this purpose of comparison with the series of other authors, an attempt was also made to regroup the tumors within the concept of gliomas introduced by Kernohan.

Histologically, the calcifications were classified into four patterns. Pattern I was the type most frequently encountered and occurred within the blood vessel walls.

Pattern II consisted of the changes described as Pattern I when adjacent blood vessels were involved whose zones of necrosis overlapped, concentric layers of calcium marking the former site of each vessel resulting in a conglomerate mass of calcium.

Pattern III consisted of calcium salts deposited in areas of old hemorrhages or necrosis.

Pattern IV consisted of several types: globules of calcium, calcific changes within the stroma of the tumor or its capsule, calcific changes at the periphery of a tumor.

On histologic examination, calcification was found in 207, or 13.1 per cent, of 1,577 intracranial tumors. Pattern I was found 93 times. Pattern IV occurred 85 times. Pattern III was observed in 20 tumors and Pattern II was noted only 9 times.

No attempt was made to correlate the microscopic calcification with roentgenographic shadows but a consideration of the major histologic patterns as demonstrated in this study may occasionally aid in the interpretation of the roentgenogram. The first pattern gives rise to a flocculent or worm-like shadow resembling the vascular pattern as it appears on the arteriogram. The second and third patterns may appear on the roentgenogram either as a single large shadow or as a solid sheet of calcium. Pattern IV includes calcium of several types and does not cast a characteristic shadow.

In children, sheets or masses of supratentorial calcium in the roentgenogram suggest the presence of an ependymoma. Calcification in the suprasellar region is highly suggestive of craniopharyngioma. In the authors' material, no definite histopathological diagnosis could be made when calcification occurred in the pineal region. Calcification in neoplasms of the posterior fossa is most suggestive of astrocytoma or ependymoma of the cerebellum.

In adults, roentgenographic correlation with the histologic tumor type is more difficult. However, in the middle-aged group, calcified tumors of the frontal region are most likely to be astrocytoma or oligodendroglioma. In those patients over the age of fifty, oligodendroglioma is the most probable lesion. Calcified lesions of the parasellar region are more prone to be craniopharyngiomas than primary neoplasm of the pituitary gland. Calcification in close association with the dura or falx may suggest the diagnosis of meningioma. This should not be confused with the physiologic calcification which occurs commonly at these sites.

The authors conclude that when calcification is visible in the roentgenogram, a consideration of these microscopic patterns and their locations, correlated with clinical data, may in certain instances suggest the histologic structure.

An insufficient number of cases were examined following roentgen therapy to ascertain whether or not any relationship exists between irradiation and the occurrence of calcification in particular tumor types.

Calcification occurred in the authors' series in every major tumor group except the schwannomas and hemangioblastomas.—*C. Peter Truog, M.D.*

ALBERTENGO, JUAN B. Síndrome tumoral del foramen magnum. (Tumoral syndrome of the foramen magnum.) *An. de cir.*, Sept.–Dec., 1952, *17*, 171–184.

According to the literature, meningioma is the most common tumor occurring in the region of the foramen magnum. The author presents a patient with neurofibroma in this region.

The first symptom is unilateral or bilateral occipital pain, which may radiate to the shoulder. The patient presented in this report had experienced suboccipital pain on awakening three years before admission. Later the pain became more intense and radiated to the right mastoid region and hemicranium. Disagreeable sensations simulating "electric currents" passed over the right side of the body down to the toes. Difficulty in writing, buttoning clothes and combing the hair were then noticed. Horner's syndrome developed. Muscular changes follow, leading to hemiparesis.

Roentgenography may reveal erosion of bone in the region of the foramen magnum. In meningioma calcification may be noted.

Spinal puncture may be dangerous in these patients. Increased pressure and high protein values may be obtained. Myelography must also be approached with caution, and unless great care is exercised the lesion may be missed.

Treatment is surgical. In the patient presented, a neurofibroma of the region of the foramen magnum and upper cervical region was found. Two operations resulted in recovery.—*Charles Nice, M.D.*

AMER, AYOUB. Approach to surgical diagnosis of the temporomandibular articulation

through basic studies of the normal. *J. Am. Dent. A.*, Dec., 1952, *45*, 668–688.

Diagnosis of pathoses and traumatic injuries of the temporomandibular joint is a difficult problem for the oral surgeon. The purpose of this study is to discover an adequate technique for roentgenographing the condyloid process and to verify the statements of standard anatomical texts with regard to the features of the condyle.

A comparative analysis was made of the various techniques used in the roentgenography of the joint, including use of a contrast medium injected into the joint. A new technique was also developed in order to survey both condyles along their long axes (lateromedial). This study included roentgenographic surveys of 35 individuals between twenty and thirty years of age, of the temporomandibular joints of cadavers, and of 20 dry specimens.

None of the standard techniques were found to be adequate and the use of a constrast medium obscured the osseous structure and outline of the condyles. The special technique which was found most useful is as follows:

A vertical, 8 by 10 inch cassette holder, which can be raised or lowered as required, is used in conjunction with an ordinary dental chair. The patient is seated in the chair with the back and head rest lowered so that a line from the ala of the nose to the tragus of the ear is perpendicular to the floor. The cassette is placed as near the top of the head as possible, the plane of the film being perpendicular to the floor, and the central ray is directed through the condyles just anterior to the ear and perpendicular to the plane of the film. The factors used are 5 foot targer-film distance, 65 kg., 15 ma., six to seven records.

The advantages of this technique over others studied are a minimum of distortion, possibility of comparison of both condyles in the same plane on a single negative, better evaluation of the relation of both joints to the structures at the base of the skull and of the extent of pathologic changes which may be present. Roentgenograms in lateral projection alone can be misleading. While the right and left condyles in the same normal individual present a wealth of variations in size, width, length and position, it was also found that such variation is within the normal range in the majority of cases.—*A. B. Smith, M.D.*

Ombrédanne, Poncet, Porcher, and Gilles. Tomographies dans les aplasies d'oreilles. (Tomography in aplasias of the ears.) *Ann. d'oto-laryng.*, 1952, *69*, 564–573.

Laminagraphy (tomography) is presented as a supplemental means of diagnosis of hypoplasia and aplasia of the ear. It is the opinion of the authors that more precision and clarity as to the structure of the inner, middle and external ears can be obtained by this method than by roentgenography in the incidences of Schüller (temporotympanic) and of Schausse (for the visualization of the inner ear) or in the occipitofrontal incidence (for the visualization of the external ear).

In aplasia, laminagraphy permits the precise determination of the absence of the external auditory meatus, the absence or presence of a fistulous tract at the tympanic ring, the absence or presence of a middle ear and its exact form and size, and the presence of the middle ear auditory ossicles. It also permits estimation of the relationship of the external auditory meatus with respect to the middle ear and meninges and the presence of the meningeal procidentia (quite frequent).

The sagittal laminagrams are of importance in the diagnosis of cholesteatoma and attic disease. These are made with sections usually 5 mm., and occasionally only 2 mm., apart. For the frontal sections in a seven year old patient, the zone of interest lies between 7 and 8.5 cm. deep from the most prominent part of the occiput, whereas for the sagittal sections it is 3 to 4 cm. deep from the skin of the external ear.

The authors use a laminagraphic apparatus describing a sinusoidal excursion.

Several reproductions of laminagrams and photographs of postoperative specimens of various ossicles of the ear accompany this article.—*J. N. Sarian, M.D.*

## Neck and Chest

Evans, William. Oesophageal contraction and cardiac pain. *Lancet*, Dec. 6, 1952, *2*, 1091–1097.

This article is an extensive study of the relationship between esophageal arrhythmia which causes chest pain simulating coronary disease and real coronary artery disease. The abnormal roentgenological signs of disturbance of swallowing are described in detail and the fluoroscopic findings are illustrated by drawings. The author elects to call the abnormal activity of the gullet esophageal arrhythmia. At times the customary rhythmical progression of the meal along the esophagus gives way to irregular movements. In this event the first portion of the meal halts, often momentarily, at the diaphragmatic opening, and some or much of it may pass into the stomach. When the next portion of the meal arrives, it is again held up, and each additional supply of barium distends the lower end of the esophagus. As the act of swallowing proceeds, the air above presses on the column of barium below and causes the tube to swell still more, but the esophageal trap holds firm, and the bulk of the meal fails to enter the stomach. The next notable event is a sharp recoil of the meal so that it is suddenly jettisoned upwards in the gullet, the lumen of which resumes its customary

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narrow caliber for a brief period. This sequence of events may be re-enacted several times before the barium is ultimately discharged piecemeal into the stomach. If the trap at the diaphragmatic opening remains closed, the esophagus may hold a tall column of barium and may not display its spectacular movements until it is partly emptied; this phase differs from the naturally sluggish esophagus where the meal passes slowly but without noticeable impediment and without recoil.

The study was begun fifteen years ago when the author began searching for the cause of pain simulating coronary disease in patients with normal electrocardiograms.

Fourteen hundred persons were selected for observation to determine the occurrence of abnormal swallowing signs in patients without definite symptoms: 700 healthy subjects, 200 patients with painless heart disease and 500 with cardiac infarctions. It was found that esophageal arrhythmia occurred in 37 out of 1400 cases (2.6 per cent). The sign occurred in 12 (1.3 per cent) of 900 cases without chest pain and in 25 (5 per cent) of 500 cases with cardiac infarction whose pain presumably was the direct outcome of coronary arterial disease. Thus it was shown that esophageal arrhythmia does occur in apparently normal persons and when it does it is without significance.

The next group studied was that of 332 patients with a clinical history suggestive of coronary disease but in whom no objective evidence of heart disease could be found. In this group evidence of esophageal arrhythmia was present in 133 (40 per cent) out of 332 cases, so that it was assumed that the origin of the pain was dyspeptic rather than cardiac. In order to confirm this assumption the patients were followed carefully over a number of years to be certain that changes in the electrocardiogram did not develop later. In only 5 cases did the electrocardiogram change. The symptoms in this group of patients responded better to remedies intended to relieve gastrointestinal symptoms than to remedies administered for cardiac disease.

The author does not think that the chest pain is the direct outcome of esophageal spasm unless it is segmental spasm. Nor does he think that disease, such as ulceration, achalasia, hiatal hernia, etc., is the source of chest pain.

The importance of recognizing the abnormal conditions of the esophagus is stressed. If this is done certain patients will be saved from becoming cardiac invalids.

This is a very important article and should be read carefully by radiologists.—*J. H. Harris, M.D.*

RESANO, J. HORACIO, and NOTTI, HUMBERTO. Estenosis congénitas del esófago; contribución a su estudio. (Contribution to the study of congenital stenosis of the esophagus.) *Prensa méd. argent.*, Nov. 21, 1952, *39*, 2915–2920.

An accurate diagnosis of congenital stenosis of the esophagus as distinguished from a congenitally short esophagus should be made for purposes of treatment. The clinical, roentgenologic, endoscopic and anatomic findings of congenital stenosis of the esophagus are characteristic, particularly vomiting of the material in the esophagram and the trap door like dysaphia to solid foods. Roentgenologically the esophagus shows an annular or canal like narrowing.

Congenital stenosis of the esophagus is a rare pathological condition. In 3,000 cases in which the chief complaint was dysaphia, only 4 cases of congenital stenosis of the esophagus were found as compared with 109 cases of congenitally short esophagus. In the first condition, the problem is a mechanical one. On the other hand, the congenitally short esophagus should be operated upon before the seventh year because regurgitation of the gastric contents into the air ways while the child is sleeping can cause a tracheo-broncho-alveolitis.

The history of congenital stenosis of the esophagus usually dates from the first month of life, with vomiting immediately after nursing. If the stenosis is not severe enough to interfere with the passage of milk, the symptoms may appear when the child begins to take solid food. Before the diagnosis of pylorospasm or pyloric stenosis is made, the esophagus should be examined for evidence of this congenital lesion. In a congenitally short esophagus, the roentgenologic-examination discloses a herniated portion of the stomach containing gastric folds. The esophagrams in one case of congenital stenosis looked as if the esophagus was tied with a thick string causing a partial obstruction and dilatation of the esophagus above this obstruction.—*Murray M. Friedman, M.D.*

MCCORT, JAMES J. Radiographic identification of lymph node metastases from carcinoma of the esophagus. *Radiology*, Nov., 1952, *59*, 694–711.

The anatomy of the lymphatic system of the esophagus is reviewed. Because of frequent spread by the lymphatic system three important questions arise: "(1) What factors bear on the frequency of lymph node metastasis? (2) Which lymph nodes are most likely to be invaded in relation to the anatomical site of the primary tumor? (3) What is the roentgenographic appearance of the lymph nodes when enlarged by tumor?"

A group was selected for detailed analysis consisting of 119 patients, of whom 80 had metastases to lymph nodes. Squamous-cell carcinoma was the predominating type of tumor. There was less frequency of early metastases in the lower grades of malignancy. It was impossible to determine the presence or absence of lymph node metastases on the basis of

the roentgenographically determined length of the lesion. No correlation between the morphological type of tumor and the presence of metastases was evident.

Considering the site of the primary tumor the following observations regarding metastases were made: (1) When the primary lesion involves the mid-thoracic esophagus there may be a slightly greater tendency for the disease to spread to the right than to the left paratracheal lymph nodes. (2) When the tumor is situated in the third and fourth segments of the esophagus, there is a high incidence of involvement of the para-esophageal lymph nodes. (3) The lower the level of the tumor in the esophagus, the more likely there are to be lymph node metastases beneath the diaphragm.

Enlargement of cervical lymph nodes is determined by palpation. Preoperative detection of enlargement of all other lymph nodes is dependent upon careful roentgenographic technique. The technique of roentgen examination is described and the value of examining the patient in both erect and Trendelenburg position fluoroscopically with barium meal is stressed.

The factors contributing to the enlargement of the various lymph node groups and the methods of detecting them are fully discussed.

The relationship of lymph node metastases to prognosis is considered and it is concluded that best results are obtained by complete surgical removal of the primary lesion and metastatic lymph nodes. Fifteen figures of descriptive roentgenograms are included.—*Everett E. Seedorf, M.D.*

Bracher, Allen N., and Koontz, Amos R. Mediastinal bronchogenic cyst and Klippel-feil syndrome; report of a case. *J.A.M.A.*, Nov. 8, 1952, *150*, 1006–1009.

The authors review the literature on bronchogenic cyst and call attention to the fact that the first true embryological bronchogenic cyst was reported in 1859 by Meyers.

This type of cyst is said to develop about the time the foregut divides into two parts: the tracheal or ventral bud, and the esophageal bud.

Bronchogenic cysts are generally found in the mediastinum and are frequently in the posterior portion of the superior mediastinum, near the bifurcation of the trachea. Only occasionally are they found to communicate with the bronchi or with the trachea. They are identified pathologically by the presence of most of the elements normally found in the walls of the bronchus. The tumors are generally round in appearance and they usually contain a clear or opaque fluid.

The authors present the case of a white male, who was seen while serving in the Army. In addition to the bronchogenic cyst, this patient showed congenital anomalies in the cervical and upper thoracic spine with fusion of the bodies of the 3rd, 4th, and 5th cervical vertebrae, with hemivertebrae and absence of the left half of the 3rd thoracic vertebra. The tumor in this case was rounded and about the size of a lemon. It was located adjacent to the left anterior margin of the lower thoracic spine. It was removed surgically without serious complications and the pathologic diagnosis was congenital cyst of bronchial origin, showing squamous metaplasia. One area of the tumor showed some similarity to the esophagus.

The predominance of ciliated epithelium, like that lining the bronchi, seemed to rule out the possibility of reduplication of the esophagus.—*R. E. Kinzer, M.D.*

Hilbish, Theodore F., and Morgan, Russell H. Cardiac mensuration by roentgenologic methods. *Am. J. M. Sc.*, Nov., 1952, *224*, 586–596.

The size of the heart is one important factor in the evaluation of the clinical status of a cardiac patient. In 1902, seeking to determine the heart size with greater accuracy, Mortiz described the methods of orthodiagraphy and teleroentgenography.

Orthodiagraphy, in which the undistorted outline of the cardiac border is recorded on the fluoroscopic screen by parallel beams of roentgen rays is probably the most precise method of cardiac mensuration, but is time consuming and requires considerable skill. Teleroentgenography, in which the roentgen tube is 6 or more feet from the 14 by 17 inch film on which the image of the heart is recorded, is a satisfactory method and magnification of the cardiac image is inconsequential, ranging from 2.5 to 5 per cent.

The four standard dimensions most commonly measured in determining cardiac size are the transverse, long and broad diameters and the frontal plane area. This last measurement is obtained by multiplying the product of the long and broad diameters of the heart by the constant 0.735.

In an attempt to determine the average values and the ranges of these four cardiac dimensions in normal individuals, 500 persons who came to the Johns Hopkins Hospital with no history of heart disease were examined by teleroentgenography. The ages ranged from two months to fifty years and approximately 100 cases were studied in each decade.

It was found that the average value for any one of these dimensions remained essentially constant after the age of twenty years had been reached. However, the wide range which occurs in each of these four cardiac measurements is striking. The normal range of the transverse diameter is greater than that of either the broad or the long diameter. The larger the range of normality the more likely it is to overlap the pathological range. The range of the frontal plane area, when compared with the range of the unidimensional measurements on similar terms, is the

smallest of the four and therefore less likely to overlap the pathological range. On this basis, the frontal plane area is the preferred measurement in cardiac evaluation.

Since the normal ranges of the cardiac dimensions are large and since these ranges considerably overlap the pathological ranges, a single teleroentgenographic examination of a patient, considered by itself, has relatively little value unless the heart is enormously enlarged. These normal cardiac ranges are not amenable to great reduction by statistical methods of correlation with physical factors associated with the patient in most cases. In view of these facts it is felt that cardiac mensuration at the clinical level should be reduced to the simplest possible terms. The authors recommend that the frontal plane area be measured and correlated with the transverse thoracic diameter which is measured at the level of the dome of the left leaf of the diaphragm. It should be noted that if this value falls within the normal range it does not necessarily mean that the heart is not enlarged. The average heart would be classified as normal until it had increased more than 38 per cent in volume. Cardiac measurements assume significance only when it is possible to compare them with those made at previous or subsequent examinations.—*A. B. Smith, M.D.*

PRUITT, RAYMOND D. Recent advances in the diagnosis of heart disease. *J. Michigan M. Soc.*, NOV., 1952, *51*, 1421–1426; also 1432.

The author discusses the advances in electrocardiography, ballistocardiography, ventricular catheterization and angiocardiography.

*Electrocardiography*. Interpretation of electrocardiograms is becoming more exact and less speculative. The diagnosis of coronary sclerosis apart from ischemia or myocardial infarction is being discarded. Stress electrocardiography is of value in determining the presence of coronary sclerosis, although 25 per cent of those with a clinically significant degree of sclerosis do not develop electrocardiographic changes while exercising or being subjected to oxygen deprivation. The relationship between the degree of coronary sclerosis and the degree of abnormality appearing in the electrocardiogram is variable. The esophageal electrocardiogram is of value in making more evident in certain instances the pathological changes that are already identified in the standard limb leads.

*Ballistocardiography* is mentioned and the author believes that significant information will result from its clinical application.

*Ventricular Catheterization Studies*. The following information is obtainable from catheterization of the right ventricle and related vascular channels: (1) pressure levels in these chambers, (2) oxyhemoglobin saturation at various points, and (3) demonstration of the presence of abnormal communications as evidenced by variants in the course taken by the catheter during the probing process. The information is of most value in diagnosing: (A) atypical patent ductus, (B) pulmonary valvular stenosis without ventricular septal defect, (C) mitral stenosis, and (D) tetralogy of Fallot. The above mentioned lesions can be amenable to surgery; they all are rare except mitral stenosis. Catheterization in mitral stenosis aids in excluding shunts, in establishing the presence of certain abnormal states characteristic of severe mitral stenosis, such as pulmonary hypertension and a low, relatively fixed cardiac output, and in providing a means for the objective study of the results of surgical procedures on the mitral valve.

A case of patent ductus arteriosus is presented in which cardiac catheterization was done. Roentgenograms are reproduced showing the catheter at the various levels, the last being in the abdominal aorta. Oxygen saturation and pressure values are also given at the various levels corresponding to the roentgenograms.

*Angiocardiography* was not used as much by the author's group as the catheterization method. However, its chief value was to demonstrate a structural peculiarity in the vascular tree at a site beyond the pulmonary arterioles which is the ordinary limit of penetration with a catheter. Coarctation of the aorta is an example. Two cases are presented with increased density in the left hilus. Angiocardiography showed that in one case this was due to the pulmonary conus and in the other to the presence of a neoplasm in the lung.

The author believes that much good will be obtained from the above advances as they are applied in the care of the patient.—*Charles W. Cooley, M.E.*

ROSENBLUTH, SIDNEY B., STEINBERG, ISRAEL, and DOTTER, CHARLES T. Abscesses of myocardium due to suppurative mediastinal dermoid: angiocardiographic and pathologic study. *Ann. Int. Med.*, NOV., 1952, *37*, 1064–1077.

The authors present a detailed report of a rare instance of myocardial abscess formation occurring from direct extension of an infected dermoid cyst of the mediastinum.—*Allison E. Imler, M.D.*

WIER, JAMES A., PICCOLI, AMO J., GREENE, DAVID G., and GREENE, CLAYTON W. Mitral stenosis with exertional cyanosis and pulmonary hemosiderosis. *Circulation*, Dec., 1952, *6*, 868–873.

This is a case report of a diffuse pulmonary hemosiderosis demonstrated by roentgenologic examination and confirmed by autopsy. The patient showed marked exertional cyanosis. There had been attacks of rheumatic fever over thirty years before the final illness. Cyanosis had been present on exer-

tion for eight years. Cardiac symptoms had been increasing for three months. Roentgen examination showed an enlarged heart, increased vascular markings and a diffuse nodulation of the lung fields. The cardiac silhouette and the physical findings were typical of mitral stenosis.

During the last month of life the cardiopulmonary function was elaborately studied and the results are tabulated.

The autopsy report is detailed. The lungs showed impressive deposits of nodular distribution of granular hemosiderin. These hemosiderin deposits were largely intra-alveolar and moderately compressed the surrounding alveoli. There were subpleural deposits of hemosiderin. Groups of cells containing hemosiderin were noted. Other findings characteristic of chronic passive congestion were shown.

A discussion of the cause of the cyanosis is given. The hemosiderosis apparently had a very mild effect on the pulmonary function and its effect on lung function is considered benign. The possible origin of the hemosiderosis is suggested.—*Edgar C. Baker, M.D.*

Overholt, Richard H., Walker, James H., and Woods, Francis M. Hidden or unsuspected bronchiectasis in the asthmatic patient. *J.A.M.A.*, Oct. 4, 1952, *150*, 438–441.

Bronchiectasis is often present in the severe asthmatic patient who fails to respond to various types of conservative therapy. Bronchospasm hampers drainage and ventilation, which increase the chronic irritative phenomena of infection while the cough and purulent or bloody sputum of bronchiectasis can cause bronchospasm. The two processes thus can augment one another in a pernicious cycle of events leading progressively to chronic and crippling pulmonary disease.

Over a period of four years ending in January, 1952, 76 severe asthmatic patients were studied in the Overholt Thoracic Clinic in Boston. Bronchoscopy was employed primarily as a diagnostic measure but also as a method of aspirating retained bronchial secretions. Bronchography was performed in 75 patients without incident although the quality of examination was occasionally unsatisfactory because of undue bronchospasm, tenacious secretions or associated respiratory distress. In spite of careful preparation including preliminary hospitalization, bronchodilators, antibiotics and bronchoscopy, repeat examinations were required in a number of instances. Twenty-seven cases of bronchiectasis were thus detected with the disease appearing bilaterally in thirteen.

In 26 patients segmental resection of diseased tissue could be performed without sacrificing undue amounts of normally functioning parenchyma. Twenty of these persons, or roughly 26 per cent of the entire group, were subsequently much improved or completely free of symptoms, and only 7 continued to require bronchodilator drugs.—*James A. Martin, M.D.*

Ettinger, Alice, Bernstein, Charles, and Woods, Francis M. Bronchial rearrangement and bronchiectasis following pulmonary resection. *Radiology*, Nov., 1952, *59*, 668–682.

The general direction of bronchial shift following segmental or lobar resection is the same as that occurring in atelectasis, except that the extent of the shift is more marked. Such bronchial rearrangement may be modified by the presence of anatomic variations or the occurrence of postoperative complications. These conclusions are based on a study of 37 resections with satisfactory preoperative and postoperative bronchograms.

Often postoperative bronchiectasis may be traced to preoperative disease, but when it apparently develops postoperatively, it is usually associated with postoperative complications such as atelectasis or pleurisy. Spatial rearrangement of the bronchi is rarely followed by kinking of the bronchi and such a factor is probably of little significance in the development of postoperative bronchiectasis.—*Martin B. Goodwin, M.D.*

Rubio, Roberto, and Piovano, Selika. Agenesia e hipoplasia bronco pulmonar. (Bronchopulmonary agenesia and hypoplasia.) *An. Fac. de med. de Montevideo*, 1952, *37*, 75–100.

The authors present 2 cases along with some considerations concerning this matter.

*Definition:* Bronchopulmonary agenesia and hypoplasia are developmental deficiencies of different degrees of the bronchopulmonary system.

*Embryology:* The development of the respiratory organs takes place in a 3 mm. embryo from a ventral ridge arising from the endoderm originating the structures that later will give rise to the larynx, trachea, bronchi and lungs. A furrow separates these structures from the gastrointestinal ones. The bifurcation of the trachea into the two main bronchi and its lining with epithelial tissue take place in the 4 mm. embryo and immediately thereafter appear two masses attached to the right main bronchus and one to the left main bronchus. During these stages the structures have become differentiated and the cartilaginous rings and fibromuscular tissue have been formed. The size of the embryo is now 30 mm. The bronchial system keeps on branching and the masses previously mentioned give rise to three lobes on the right side and two on the left side. In the six month fetus the growing vessels interrupt the epithelial lining of the bronchial ends, thus forming the alveo-

lus and its vascular bed. Seventeen generations of bronchial branching occur until birth, the branching continuing through the first year of life to twenty-four generations. The surrounding mesoderm adapts its form to the bronchial tree in a gradual manner, forming the external lobulations of the lungs. The lung tissue, which is compact and solid at the beginning, turns gradually to a more spongy and lighter structure due to the vessels and alveolar development.

*Etiology and Pathogenesis:* These are unknown, but the pathological study of the specimens usually indicates when the arrest of growth occurred.

*Classifications:* That of Foster Carter is based on anatomical considerations and that of Puriel and Epifanio on embryological considerations.

*Foster-Carter Classification:*

I. Abnormalities of lobulation
   a. Additional fissures
   b. Absence of fissures
   c. Extra fissures due to abnormal displacement of structures
      (1) Azygos lobe
      (2) Sequestration of the lung due to an abnormal vessel
      (3) Fissure of the subclavian artery
II. Abnormalities of bronchi
   Supernumerary bronchi
   b. Displacement of bronchi
   c. Congenital cysts
III. Abnormalities of parenchyma
   a. Accessory lungs
   b. Agenesia of the lung
   c. Hypoplasia of the lung

There are also associated abnormalities.

*Puriel and Epifanio Classification:*

I. Malformation of the bronchoalveolar system
   a. Agenesia. Agenesia of one main bronchus . . . pulmonary agenesia
   b. Hypoplasias. Bronchial hypoplasia
      Pulmonary agenesia
      Bronchiectasis with bronchoalveolar agenesia
   c. Dysplasias
      Absence or alteration in the development of one or several elements of the bronchi, cartilage, muscle, etc.
      Bronchiectasis
   d. Hyperplasias. Lung cysts
      Simple
      Multiple polycystic lung

Association of congenital malformations
   Kidney, heart, gastrointestinal tract, skeleton, Morelli syndrome

*Conditions That May Be Labeled Acquired or Congenital:*

Subpleural blebs
   Fisher scar type
   Miller bleb
   Letull's congenital bronchiectasis
   Morelli dysgenesia
Emphysematous blebs or ampullar emphysema
   Bronchial ball-valve mechanism
      Congenital atresia
      Stenosis
         Tumoral
         Inflammatory
         Foreign body
   Dystrophy of the connective tissue
   Vascular abnormality

*Clinical Picture:* The left side is more commonly affected. The diagnosis is more frequently made during the first year of life; the remaining cases are picked up in the three following decades.

The clinical signs may be completely absent and the diagnosis is made accidentally either from a survey film or at a postmortem examination. The most frequent symptom is either dyspnea or orthopnea on exertion. Cyanosis, when present, is found more often in children. Hemoptoic sputum to massive hemoptysis may be seen. The chest is usually symmetrical, although there may be some asymmetry. The entire mediastinum is shifted toward the malformed side. Other congenital anomalies may be present.

*Roentgen Findings:* Anteroposterior and lateral roentgenograms of the chest show increased density of the malformed side due to mediastinal shifting. The intercostal spaces are narrower and the diaphragm is elevated. Roentgenograms with higher kilovoltage and laminagrams give the same findings.

The most important diagnostic procedures are bronchography and bronchoscopy. The first procedure demonstrates dilatation of the bronchi and absence of the alveolar pattern. Sometimes the complete absence of a main bronchus is seen as in agenesia or an underdeveloped bronchial system. Bronchoscopy shows deviation of the trachea, abnormal bifurcation, stenosis, etc.

Other procedures that may help are angiocardiography, electrocardiography and study of the respiratory capacity.

*Prognosis:* If the patient survives the first year of life, there is good probability that adulthood may be attained. The cause of death may be other than the congenital disease. These persons are apt to lose their respiratory balance easily and so acquire superimposed infections.

*Treatment:* Treatment according to Clagett is as follows:

a. If no symptoms are present: follow-up.

b. If the symptoms are slight: follow-up.
c. In case of important complications such as infections, hemoptysis, etc.: surgical treatment.

The authors' 2 cases are described in detail.—*Julio Toriello, M.D.*

Barden, Robert P. The interpretation of some radiologic signs of abnormal pulmonary function. *Radiology*, Oct., 1952, *59*, 481–488.

Abnormalities in pulmonary function may be present even with minimal demonstrable anatomical changes. Careful fluoroscopic examination of the chest and roentgenograms in full inspiration and full expiration are necessary to demonstrate these changes. Additional information can be obtained by bronchography and angiocardiography and roentgenograms made with the Potter-Bucky diaphram.

Emphysema may be manifest on roentgenograms of the chest by localized or diffuse areas of overinflated lung. These areas do not deflate normally at full expiration and show a disturbed pattern of pulmonary markings. Fluoroscopic examination and roentgenograms made in the lateral projection are essential.

Arteriolar sclerosis is a common degenerative condition in the lung as well as in the rest of the body. The essential findings are enlargement of the main pulmonary arteries and the disappearance of the finer lung markings.

Localized occlusion of large pulmonary vessels may result in an area of consolidation due to hemorrhage into the lung tissue. Hemorrhage into the area may not occur, however, or may be delayed. In this event roentgenograms show an area devoid of lung markings. The appearance may resemble that seen in localized emphysema.

When pulmonary arteriovenous fistula is present, final diagnosis depends on the demonstration of the fistula by means of angiocardiography. Routine roentgenograms may show little or no anatomic abnormality. The findings of one or more nodular shadows in the pulmonary fields should arouse suspicion of an arteriovenous fistula, especially if hemoptysis or compensatory polycythemia is present.—*Arno W. Sommer, M.D.*

Williams, Mark H. Localized pulmonary hypertrophic emphysema. *J. Thoracic Surg.*, Nov., 1952, *24*, 522–529.

Localized pulmonary hypertrophic emphysema is an extraordinarily rare type of cystic disease of the lung. All of the 9 well documented examples of the disease thus far published have occurred in infancy or early childhood.

The author reports a case of an infant having massive hypertrophic emphysema of the right middle lobe on whom a successful lobectomy was performed.

The literature relevant to this disease is reviewed, and the clinical, roentgenologic, and pathologic data are summarized. Chest roentgenograms of 8 patients were made. In every instance these studies demonstrated hyperaeration of the affected lung with decreased markings, mediastinal displacement toward the opposite side, various degrees of depression of the diaphragm and widening of the interspaces of the involved hemithorax.

Seven of the 9 cases reported in the literature were subjected to lobectomy or segmental resection without mortality. The available information indicates that the disease is a clinical entity of congenital origin, and that resection should be done promptly when the diagnosis is made.—*Thomas C. Stansbury, M.D.*

Barrett, N. R., and Thomas, Dillwyn. Pulmonary hydatid disease. *Brit. J. Surg.*, Nov. 1952, *40*, 222–244.

This is a detailed account of the authors' experience with 71 cases of pulmonary hydatid disease (echinococcosis) from 1938 to 1952, indicating how their theories of the pathogenesis of the disease have led them to evolve a rational surgical approach to the condition. They hold no brief for conservative medical approach to the disease—indeed, none of the available drugs appear to be truly parasiticidal.

The growing cyst has a germinal membrane which lays down a tough, laminated hyaline capsule acting as its envelope. These hyaline sheets are laid down continuously, the oldest on the outside of the sphere, and form an integral part of the cyst. However, they are completely and easily separable from the adventitial zone of the host. This circumstance enables the surgeon to enucleate the intact cyst very readily, provided that no secondary infection has obliterated the cleavage plane. The authors describe their meticulous enucleation technique, and warn that spilling of the cyst contents into lung or pleural space causes spread of germinal membrane, brood capsules and scolices, giving rise to daughter cysts in the lung, pleural cavity or incision. However, for some unknown reason, extrusion of cyst fluid via the bronchial tree does not cause bronchial dissemination of parasites, although spillage by any route may provoke marked allergic reaction (anaphylaxis) in the host.

The "simple" (uncomplicated) pulmonary hydatid cyst typically grows to extreme size without causing pulmonary symptoms, owing to its gradual displacement of bronchi and vessels. However, the stretching of adjacent parenchyma may cause small bronchial fistulas, from which small quantities of air leak into the cyst adventitia, dissecting into the space between it and the laminated hyaline membrane of the cyst. A characteristic pericystic, perivesicular halo of air is then noted on the roentgenogram, in the form of a crescentic or scimitar-shaped bubble which may be

made to outline the entire cyst circumference by moving the patient from upright into lateral decubitus and inverted positions. This "perivesicular pneumocyst" is considered to be a pathognomonic sign of hydatid lesion, when it can be demonstrated.

Following enucleation of a pulmonary hydatid cyst, minute bronchial fistulas may cause persistent tension pneumocysts or pneumothorax, although most frequently the empty adventitial capsule closes spontaneously, obliterating itself without complication.

Various complications are discussed, such as partial or complete cyst rupture; secondary infection; and retention of membranes following rupture, leading to abscess.—*Stanley M. Rogoff, M.D.*

WYMAN, STANLEY M., and EYLER, WILLIAM R. Anomalous pulmonary artery from the aorta associated with intrapulmonary cysts (intralobar sequestration of lung); its roentgenologic recognition and clinical significance. *Radiology*, Nov., 1952, *59*, 658–667.

Embryologically, an anomalous pulmonary artery arising from the aorta, either above or below the diaphragm, may be formed and supply a part of the posterior portion of one of the lower lobes. When this supplied portion is not normally connected with the bronchial tree it is called "intralobar sequestration of lung." Hiatus hernia is a frequently associated condition.

Seven surgically proved cases which fall into two distinct clinical and roentgenographic types are presented.

Three cases were asymptomatic and found incidentally. In these, a sharply delineated homogeneous mass was seen involving the posterior, medial or inferior part of a lower lobe with a finger-like projection directed toward the aorta, and occasionally piercing the diaphragm.

Four patients showed recurrent lower lobe infection, and in these, thin-walled cysts were present in the posterior basal portion of the lower lobe. At times, air-fluid levels were seen in the cysts, and they may be obscured by adjacent consolidation. Recurrent infections in the same part of a lower lobe and mild general illness of the patient in contrast to the marked consolidation are characteristic of the condition.

The roentgenographic importance is to be able to warn the surgeon of the possibility of inadvertent section of the anomalous artery which usually anastomoses with the normal pulmonary arteries.—*William A. Goodrich, M.D.*

SHIELDS, D. O., CHAPMAN, JOHN S., JR., CARSWELL, JAMES, JR., and WOLLENMAN, O. J. Nodular tuberculosis. *J. Thoracic Surg.*, Dec., 1952, *24*, 568–577.

During the past few years resection of nodular tuberculosis has been common. Medlar has shown that the center of the nodule is caseous and is often in close relationship with a bronchus. Owing to the fact that prolonged bed rest, antibiotics and collapse therapy usually have little effect on nodular lesions and since the possibility of central liquefaction, cavity formation and spread is real, even after prolonged periods of inactivity, surgical resection is definitely indicated in certain forms.

Nodular lesions may develop from clearing tuberculous pneumonia, by cavities becoming inspissated and by the formation of true tuberculomas. Many times the mode of development is unknown.

A group of 140 cases of nodular tuberculosis was followed for an average period of four years without resorting to surgical resection, and in 25 per cent reactivation was noted. The highest incidence of reactivation was in multiple nodular tuberculosis and in nodular lesions produced by inspissated cavities. Nodular residuals of clearing tuberculous pneumonia and of unknown development had a low incidence of reactivation. Lesions over 1 cm. in diameter did not have a significantly higher rate of reactivation than lesions under 1 cm. in diameter. Cases followed from six to twenty-seven months showed no greater difference in percentage of reactivation than those followed longer than twenty-seven months.

Thirty patients with nodular tuberculosis were subjected to surgical resection and after an average follow-up period of twenty-seven months, only 2 patients, or 7 per cent, were found to have developed signs of reactivation.

The authors believe that resection should be limited to the form produced by inspissated cavities and to the multiple nodular tuberculosis.—*Paul C. Olfelt, M.D.*

LACKEY, ROBERT W., LEAVER, FRANK Y., and FARINACCI, CHARLES J. Eosinophilic granuloma of the lung. *Radiology*, Oct., 1952, *59*, 504–513.

Two histologically proved cases of eosinophilic granuloma limited to the lungs are reported. An additional case of eosinophilic granuloma of bone with pulmonary findings is also described.

The roentgen picture was identical with that of Letterer-Siwe disease, Hand-Schüller-Christian disease, Gaucher's disease, and the other xanthomatoses. In both cases there was generalized widespread nodular infiltration of the lungs. The nodules varied in size from miliary dimensions up to 1.5 cm. in diameter; they were not sharply circumscribed. Localized areas of emphysema and fibrosis were associated with the nodular infiltration.

The clinical manifestations were mild. Both cases complained of mild cough. There was low grade afternoon temperature.

In the differential diagnosis it is necessary to consider all conditions which give rise to (a) diffuse nodular granulomatous pulmonary infiltrate, (b) pulmonary fibrosis, and (c) emphysema of scattered segmental type.—*Arno W. Sommer, M.D.*

Doll, Richard, and Hill, A. Bradford. A study of the aetiology of carcinoma of the lung. *Brit. M. J.*, Dec. 13, 1952, *2*, 1271–1286.

This article is a statistical analysis of nearly 1,500 cases of carcinoma of the lung, and an equal number of controls, with regard to numerous factors which have been suggested as causative agents such as smoking, place of residence, inhaling, use of filters or lighters, kind of cigarettes, etc.

Of 1,357 men with carcinoma of the lung, 0.5 per cent were non-smokers and of 108 women 40, or 37 per cent, were non-smokers. The corresponding figures in the control group were 4.5 per cent for men and 54.6 per cent for the women. Of the men with lung carcinoma 25 per cent had been smoking 25 or more cigarettes a day. The corresponding figure for the control group was 13 per cent.

The article concludes that there is a real association between smoking and carcinoma of the lung. The authors do not state that all cases of the disease are related to smoking.

This study is based on elaborate questionnaires and comprises an impressive number of cases. In view of the current controversy on the subject, these figures will be of help in future evaluation of factors connected with carcinoma of the lung.—*George L. Sackett, Jr., M.D.*

Rigler, Leo G., O'Loughlin, Bernard J., and Tucker, Richard C. Significance of unilateral enlargement of the hilus shadow in the early diagnosis of carcinoma of the lung; with observations on a method of mensuration. *Radiology*, Nov., 1952, *59*, 683–693.

Earlier diagnosis is obviously necessary to increase the cure rate of bronchogenic carcinoma. Unilateral enlargement of the hilus is a frequent and important early, presymptomatic sign. Since the problem is not one of diagnosis, but one of detection, a method of mensuration of the roentgen shadow of the hilus is described.

The medial border of the hilus is arbitrarily fixed by a vertical mid-thoracic line bisecting the horizontal transthoracic diameters at the aortic arch and at the diaphragm. The most lateral margin of the hilar shadow as it encroaches upon the aerated lung fields is then located. With these points of identification it is possible to measure the right and left transverse diameter of the hilus and determine the sum of the transverse diameters.

The authors made hilar measurements on 127 patients with proved carcinoma of the lung and on a group of 100 patients selected for control studies.

Observations and sources of error are discussed in detail. A few of the important conclusions are as follows: A transverse hilar measurement of 5.7 cm. or less is clearly indicative of normal. A measurement of 7.0 cm. or more is indicative of an abnormal hilus. Between the transverse hilar measurements of 5.7 to 7.0 cm., 11 per cent were normal, but 42 per cent were abnormal.

If the sum of the diameters of the hiluses is under 11.0 cm., there is little chance of carcinoma being present; but if the sum exceeds 13.0 cm. there is less than a 10 per cent chance that the subject is normal. If the difference between the right and left hilus is greater than 1.7 cm., there remains only a 10 per cent chance of the larger of the two being normal.

The reader is reminded that these figures are only an aid and do not supplant the critical judgment of the experienced roentgenologist. The article is illustrated with graphs and descriptive roentgenograms.—*Everett E. Seedorf, M.D.*

Kergin, Frederick G. Silicotic and tuberculosilicotic lesions simulating bronchiogenic carcinoma. *J. Thoracic Surg.*, Dec., 1952, *24*, 545–567.

It has been known for a long time that patients suffering from pulmonary silicosis with or without added tuberculosis may show areas of density in chest roentgenograms which may be mistaken for bronchiogenic carcinoma developing in a background of silicosis.

Eight patients are presented, 7 of whom did not exhibit the usual roentgenographic picture of silicosis. All had a unilateral density, segmental or lobar in extent, as is often seen in bronchiogenic carcinoma, but which in fact was due to silicosis. All 8 patients were men in the middle age group with complaint commonly associated with bronchiogenic carcinoma. Almost all had a history of exposure to dust. Seven of the 8 were operated upon and the diagnosis confirmed histologically. The fundamental pathological feature in this group of patients was found to be a complete or partial bronchial obstruction due to pressure by enlarged lymph nodes, which are the site of a chronic inflammatory reaction secondary to silica-containing dust. In 3 of the 8 patients, there was an added tuberculous infection.—*Paul C. Olfelt, M.D.*

## Abdomen

Massion, J., Everarts, P., and Leroy, F. Premiers essais de cholécystographie au moyen du télépaque. (First use of telepaque in cholecystography.) *Acta gastro-enterol. belg.*, Nov., 1952, *15*, 743–647.

Telepaque was used in 40 cases in doses of 5 to 6 grams. Tolerance was good to excellent in most subjects and was superior to that observed with previously used agents.

Five times an excluded gallbladder permitted entry of the drug and in 4 of these a calculus could be diagnosed with certainty. Gallbladder opacity was excellent in all and in more than half, the biliary tracts were outlined.—*Marcy L. Sussman, M.D.*

LOPES PONTES, J. P., and CAMINHA, NICOLA. Estudo radiológico do esvaziamento da vesícula biliar em 50 indivíduos normais (observações sobre a chamada prova de Boyden). (Roentgen study of the emptying of the gallbladder in 50 normal individuals; observations on the so-called Boyden test.) *Rev. brasil. med.*, Oct., 1952, *9*, 679–689.

The purpose of this study was to determine the normal cholecystographic pattern of the emptying of the gallbladder following the ingestion of the fatty meal recommended by Boyden. The fatty meal consisted of three egg yolks mixed with 100 grams of milk and some sugar. The contrast medium employed was biliselectan (Schering).

All persons received twelve tablets of 0.5 gm. each of the contrast medium, one-half hour after the evening meal before the day of examination. The first cholecystogram was taken at 8:30 in the morning and was followed by additional cholecystograms taken 15 minutes, 30 minutes, 60 minutes and 120 minutes after the ingestion of the fatty meal. The subjects selected at random for this study (30 men and 20 women) varied in age from sixteen to forty-three years (averaging 22 years, 9 months) and belonged to the clerical staff of a local commercial company, thus representing people of the financial and nutritional middle class of Rio de Janeiro. Variations in the size of the gallbladder were observed independently by the two authors and were also determined by volumetric measurement of the gallbladder image, by using a simplified modification of Boyden's original method.

In all initial examinations the gallbladder shadow appeared normal with regard to configuration, size, density and position. No cases of calculi were noted. In only 5 of the subjects examined (10 per cent) was there evidence of a complete or almost complete evacuation of the gallbladder within two hours after the ingestion of the fatty meal. In 10 others (20 per cent) the two hour residue ranged from one-sixth to one-fourth of the pre-meal gallbladder size. In the majority of the cases (34 subjects, or 68 per cent of the entire group) the gallbladder shadow two hours after the fatty meal still measured almost one-half or over one-half of the original size. Spontaneous opacification of the common bile duct occurred in 16 persons (32 per cent of the examined total).

No correlation could be established between the cholecystographic findings and the age or clinical habitus of the subjects examined. However, somewhat more frequent two hour residues were noted in women (83 per cent as compared to 66 per cent in men). No subjective disturbances (nausea, pain) were present in a single case.

The results obtained emphasize the lack of sound criteria for the diagnosis of pathologic changes of the gallbladder function, especially as regards the so-called "gallbladder stasis" since there is an extreme variation of the gallbladder activity in the normal individual. The present concepts regarding biliary dyskinesia, as demonstrated by cholecystographic examination, seem to be entirely inadequate, and therefore necessitate further investigation and possibly a radical revision.—*Ernst A. Schmidt, M.D.*

BARAVALLE, NORBERTO, and TORRES, LUCIANO M. Patología del colédoco. (Pathology of the common bile duct.) *An. de cir.*, Sept.–Dec., 1952, *17*, 119–132.

Operative and postoperative cholangiography are of established value in studying patients with diseases of the biliary tract. The detection of stones in the common duct is of great importance. Dystonia of the sphincter of Oddi may result in retarding the passage of the opaque medium into the duodenum. In the latter condition, the opaque medium is frequently seen to flow backward into the pancreatic duct, thus explaining the pathogenesis of pancreatitis in some patients. Manometrical study may indicate a state of increased tension in the common duct.

An inflammatory process may involve the terminal portion of the common duct, and in some patients this results in sclerotic changes. Papillotomy is necessary in such cases.

Most patients revealing increased tension or spasm in the common duct will be found to improve spontaneously in time. Postoperative cholangiography is important in studying these patients.—*Charles Nice, M.D.*

TORRES, LUCIANO M. Colecistitis alitiásicas. (Cholecystitis without stones.) *An. de cir.*, Sept.–Dec., 1952, *17*, 202–220.

Cholecystitis without formation of gallstones may be due to various causes. In spasm near the papilla or sphincter of Oddi pancreatic ferments may gain entrance into the upper biliary tree. These ferments have been found in as high as 53 per cent of gallbladders presenting cholecystitis without stones. Parasitic infections such as lambiasis and distoma hepaticum may give rise to ascending infection of the biliary tree. Lesions of the gallbladder, neck of the gallbladder and sphincters may give rise to biliary stasis, allowing cytolytic action of bile salts of the latter; taurocholate and desoxycholic acid have been found to be twice as active as sodium glycolate.

Epidemic hepatitis may be followed by cholecystitis.

Diagnosis depends on the clinical picture, duodenal drainage studies and cholecystography. Therapeutic measures include medical therapy to stimulate biliary drainage, at times antibiotics, and surgical measures.

Ten case reports and reproductions of roentgenograms are given to illustrate the clinical study and treatment of these patients.—*Charles Nice, M.D.*

Borron, Randolph W. J., Goldberg, Leonard, and Knowlton, Charles E. Polyp of the duodenal bulb; report of a case. *Radiology*, Oct., 1952, *59*, 570–572.

The authors report the finding of a solitary polyp within the duodenal bulb on roentgen examination. The incidence of duodenal polyps is low, this case increasing to 22 the number which have been described in the literature.

The operative and pathological findings are discussed. The patient made an uneventful recovery following surgical removal of the polyp.—*Everett E. Seedorf, M.D.*

Baker, Lester, and Spellberg, Mitchell A. Pyloric stenosis secondary to hydrochloric acid ingestion; report of two cases in which hepatitis developed. *J.A.M.A.*, Oct. 4, 1952, *150*, 442–446.

Ingestion of concentrated mineral acids frequently results in severe gastric damage with minor infrequent damage to the esophagus. Strong alkalies, on the other hand, usually produce severe esophageal injury with stenosis, but are apparently neutralized by grastric contents and seldom injure the stomach.

Two cases of hydrochloric acid ingestion are reported in some detail by the authors. In both instances symptoms of progressive gastric obstruction developed with nausea, hematemesis and weight loss reaching a maximum severity in approximately six weeks. Cytological and blood chemical studies were probably not directly altered but both cases exhibited absence of free gastric hydrochloric acid after histamine. Roentgen examinations revealed symmetrical narrowing or absence of filling in the distal stomach with associated gastric stasis—an appearence consistent with infiltrating antral neoplasm and obstruction. At laparotomy both cases exhibited thickening and scarring with marked narrowing of the pylorus and antrum, and each patient became asymptomatic following construction of a posterior gastroenterostomy. It may or may not be coincidence that both patients required subsequent care owing to the development of homologous serum hepatitis.

In discussing therapy measures, the authors consider an acute phase in which the gastric wall may be friable and edematous introducing the danger of spontaneous perforation and precluding direct gastric surgery. Suggested treatment includes supportive measures with control of sepsis, hemorrhage, fluid balance and nutrition. In the late obstructive phase the symptoms can be relieved by gastric resection or by gastrojejunostomy if technically feasible.—*James A. Martin, M.D.*

Kleitsch, William. Diagnosis and treatment of pyloric hypertrophy in the adult. *A.M.A. Arch. Surg.*, Nov., 1952, *65*, 655–664.

A series of 4 cases of hypertrophy of the pyloric sphincter is presented. The author feels that the condition prevails more frequently than is generally appreciated. He also feels that the roentgen findings are characteristic; an elongated and narrowed pyloric canal with thickened sphincter muscle which gives the impression of a filling defect surrounding the pyloric antrum. This characteristic elongation and narrowing of the pyloric canal has been termed "pyloric string sign." Treatment is surgical.—*F. B. Markunas, M.D.*

Porcher, P. Radiographie des parois gastriques par le double contraste gazeux. (Roentgenography of the gastric walls by means of gaseous double contrast.) *Arch. mal. app. digest.*, Nov., 1952, *41*, 1049–1053.

The author reviews the difficulties inherent in gastric visualization by standard procedures and discusses a method of double contrast by use of pneumoperitoneum plus gaseous distention of the stomach. The roentgenographic technique is described with both plain films and with laminagrams.

A brief review of the pertinent literature is included. The first reference to such double contrast work was in 1920, but the first practical application was in 1933 by Makoto Saito.

The author states that between 1,200 and 1,600 cc. of gas is introduced into the abdominal cavity and that approximately 200 cc. of gas is produced in the stomach by administering a solution of a tartrate or a bicarbonate. It is impossible to visualize the entire organ in any one projection, but by manipulation of the patient into various positions and by use of fluoroscopy, all areas of the stomach can be satisfactorily studied. He feels that laminagraphy is of particular benefit when applied to the fundus.

Four illustrations are included demonstrating small lesions of various portions of the gastric wall.—*P. B. Parsons, M.D.*

Morin, Guy. Technique pratique d'insufflation digestive. (Practical technique of digestive insufflation.) *Arch. mal. app. digest.*, Nov., 1952, *41*, 1054–1057.

This paper is in the form of a preliminary report concerning the combined use of barium suspension and a dry effervescent powder. Illustrations of the double contrast study of the esophagus and stomach with the combination of these two agents are included. It is frequently possible also to visualize the duodenal bulb by double contrast.

In reviewing the subject of combined visualization, the author states that the use of effervescent powders in solution sometimes distorts the opaque medium and that introduction of gas by means of instrumentation through the esophagus is subject to some discomfort to the patient.

There are included in the article, illustrations showing a hiatus hernia before and after insufflation and double contrast films of the stomach and esophagus.—*P. B. Parsons, M.D.*

GLAZEBROOK, A. J., and WRIGLEY, FRED. A teaspoonful of baking-soda. *Lancet*, Dec. 6, 1952, *2*, 1097–1100.

In spite of many good reasons why patients with low gastric HCl should never take alkalies, the fact remains that some such patients are relieved of their distress by taking ordinary baking soda. This is true mostly of patients who have had gastric surgery for supposed duodenal ulcer.

The authors studied a number of these patients by means of dextrose barium meal with and without the addition of soda. It was found that the spasm and hypermotility of the small intestine were definitely reduced by the use of soda. The effect of soda was very similar to the effect of atropine and related compounds.

It is suggested that these patients may have a deficiency in the production of bile and pancreatic juice, hence the benefit from added alkali to the digestive juices in the small bowel.—*J. H. Harris, M.D.*

LOCKWOOD, IRA H. Lymphosarcoma of the gastrointestinal tract. *J.A.M.A.*, Oct. 4, 1952, *150*, 435–437.

Surgical intervention is the most valuable method of primary attack in treatment of malignant lesions of the gastrointestinal tract. When such lesions are determined to be lymphosarcoma, either reticulum cell sarcoma or malignant lymphocytoma, properly conducted radiation therapy constitutes an indispensable adjunct to the surgery.

Recognition of such lesions is often difficult and depends partially on knowledge that early pain, often colicky in nature, is common and is the result of involvement of submucosal nerve plexuses. Other common findings include weight loss, mild secondary anemia, achlorhydria, signs of progressive obstruction and a palpable abdominal mass. There are no pathognomonic roentgen changes, although the diagnosis may be entertained in the presence of an infiltrating lesion with diminished peristalsis and fixation of the stomach or a long lesion of the small intestine producing destruction of the mucosa with irregular widening rather than narrowing of the intestinal lumen. The prognostic outlook seems to be more dependent upon site of the lesion than histological type, the cecal lesions having the best survival records and rectal lesions the poorest. Complete surgical extirpation of the lesion and involved lymph nodes, whenever possible, followed by adequate irradiation of the tumor bed and lymph drainage areas is the desirable plan of therapy.

In the author's opinion, results of treatment with nitrogen mustard have been generally disappointing when reserved for roentgen refractory lesions, and the use of radioactive isotopes has not been significantly successful in this field. These and other points are illustrated in reports of 3 cases of lymphosarcoma and 1 of myofibrosarcoma involving the gastrointestinal tract.—*James A. Martin, M.D.*

SMITH, DONALD R., STEINBACH, HOWARD L., LYON, RICHARDS P., and STRATTE, PAUL B. Extraperitoneal pneumography. *J. Urol.*, Dec., 1952, *68*, 953–959.

The authors utilize the procedure of Rivas and others for the retroperitoneal insufflation of oxygen.

The needle is placed just below the tip of the coccyx in the midline and directed in the fascia between the rectum and the tip of the sacrum. For the right-handed operator, the patient usually lies on the right side during this injection. Where a bilateral distribution of the air is desirable, the patient lies in the prone position with the head and shoulders elevated about 15 degrees. Oxygen is then forced into the retroperitoneal tissues through water bottles, using a pressure of approximately 20 cm. of water. Usually, 1,000 to 1,200 cc. of oxygen is sufficient. The total amount used will depend on the size of the patient.

The authors have not had any untoward reactions from the technique as they have employed it, but it is pointed out that venous gas embolism is a definite serious possibility. It has been demonstrated experimentally that the cause of death in venous embolism is mechanical blockage of the outflow tract of the right ventricle by the air. This can be avoided in animals by maintaining the animal on the left side. If symptoms of embolism have developed, by placing the animal on the left side, a fatal outcome can be prevented.—*George W. Chamberlin, M.D.*

MUSGROVE, J. E. Unusual roentgenographic findings in gangrenous appendicitis. *Canad. M.A.J.*, Dec., 1952, *67*, 666–667.

A case of gaseous gangrenous appendicitis with a positive helpful roentgen finding is reported.

The case is that of a white farmer, aged thirty, who began to complain with epigastric pain. Eighteen

hours later this settled in the right lower quadrant of the abdomen. Relevant laboratory findings were leukocytosis and increased sedimentation rate. A retrocecal gas-filled appendix was seen on the plain roentgenogram and was helpful in differential diagnosis and election of site of surgical approach.—*F. B. Markunas, M.D.*

Spencer, R. Intestinal obstruction in the newborn associated with faulty development of the midgut and its mesentery; a description of three cases. *Surg., Gynec. & Obst.*, Nov., 1952, *95*, 568–578.

This article presents 3 case reports of acute intestinal obstruction in the newborn. These cases are grouped together because they have one common feature, namely inadequate fixation of the midgut and its mesentery to the posterior abdominal wall. All 3 infants were found to have some kind of volvulus of the intestine and the third was complicated by atresia or stenosis of the intestine.

At about the fourth week of intrauterine life the midgut is herniated through the anterior abdominal wall at the umbilicus. During the tenth week it returns to the peritoneal cavity from the hernial sac. The process of returning is an orderly one and it is at this stage that the final disposition of various portions of the midgut is established. Normally, the proximal loops re-enter the abdomen first and are directed posteriorly and downward behind the superior mesenteric artery. The last to re-enter is the cecum. If, however, this process of rotation does not occur, the whole of the midgut is returned to the peritoneal cavity en masse. This results in an infantile disposition of the viscera, and the normal posterior fixation of cecum and ascending colon does not occur. The whole midgut is suspended from the posterior abdominal wall by a mesentery which has very limited vertebral attachment. The cecum is in the midline or toward the left of the abdomen and the ileum opens into its right aspect. The portion of the colon which would normally be called transverse anatomically, runs downward on the left side into the descending colon and sigmoid. This large mass of intestines and colon suspended from the posterior abdominal wall by a narrow pedicle and without the normal parietal fixations easily undergoes torsion. When torsion occurs the narrow mesentery containing the superior mesenteric vessels is twisted like a corkscrew and compresses the third portion of the duodenum.

The most important diagnostic aid in detecting this type of intestinal obstruction (*i.e.*, that associated with faulty development of the midgut and its mesentery) is roentgenography. The gas distended stomach and duodenum with absence of gas in the intestines below the duodenum is strong evidence of a complete obstruction.

The author emphasizes the importance of recognizing the condition when vomiting and feeding difficulties occur in early infancy. In some of the milder cases, spontaneous regression of symptoms may take place but the congenital anomaly remains and at a later period—late childhood and adult life—may account for obscure dyspepsia and abdominal pain.—*Mary Frances Vastine, M.D.*

Jolleys, Ambrose. The diagnosis of intestinal obstruction in the newborn. *Brit. J. Surg.*, Nov. 1952, *40*, 201–210.

Over a three year period the author collected 18 cases of intestinal obstruction in newborns, occurring within one month of birth. The chief causes of such obstruction are, in order of frequency: (1) disorders in fetal rotation of the gut, encouraging volvulus; (2) intestinal atresias; (3) "neuromuscular dysfunction" such as megacolon, but which may occur in the ileum as well; (4) meconium ileus, generally associated with fibrocystic disease of the pancreas.

Less common causes are: strangulation of an internal or external hernia; volvulus associated with Meckel's diverticulum; annular pancreas; or reduplication of any portion of the bowel. Inflammatory adhesive bands may also be responsible for the obstruction.

The paper contains a simple verbal and diagrammatic description of the process of fetal gut rotation and the major aberrations encouraging obstruction. Volvulus resulting from deficient or "reversed" rotation in probably easily reduced, but the surgeon must be on the alert for associated anomalies such as duodenal atresia and congenital duodenocecal bands. In the commonest variety of deficient rotation (small bowel in the right abdomen, cecum on the left) it is wise to leave the cecum on the left side without attempting any major rearrangement of the bowel after reduction.

The author warns that intestinal atresia may be present in multiple areas, and when one such point is found, others must be searched for distally before the abdomen is closed. The ileum is the commonest site of intestinal atresia, and the resulting obstruction usually produces considerable abdominal distention. However, the duodenum is another frequent site of involvement, and in such cases the abdomen may not be distended significantly. Most commonly, duodenal atresia is at a level below the ampulla of Vater so that the vomitus is bile-stained and the meconium light-colored. Such patients may also have an hypertrophied common bile duct and may be jaundiced. When the atresia is above the ampulla, bile is not apparent in the vomitus but can be found in the meconium—if the biliary system is normal.

In "meconium ileus," the fibrocystic pancreatic disease causes deficient digestion of the mucous secretions of the alimentary tract. Hence chemical tests of the meconium indicate a predominance of

undigested viscid mucoproteins, in contrast to the more normal mucopolysaccharides and water-soluble nitrogenous compounds. *Obstruction of the ileum by these viscid plugs causes the colon to appear hypoplastic, and probably accounts for most cases of reported "microcolon."*

There is a concise section discussing the diagnostic measures used to identify these various conditions. Plain roentgenograms of the abdomen should be examined with the following view in mind: Normally air enters the stomach immediately after birth, traveling down the small intestine to be demonstrated in the colon within four hours. The level of obstruction may be difficult to detect on the film, since the infant small bowel does not have gradations in valvular pattern to help the examiner, and is amorphous in roentgenographic appearance when distended. A small barium enema can usually be performed with safety to help identify the status of the colon at least. *Radiologists are cautioned not to fill a dilated colon with an appreciable quantity of barium suspension if it cannot be expelled (as in megacolon), since the huge water volume introduced per rectum in order to pack a megacolon may lead to serious water intoxication.*

In meconium ileus, the vomitus will be deficient in pancreatic ferment. The absence of trypsin is used to advantage in the following diagnostic test: A strip of unprocessed film is inserted into the vomitus. "If trypsin is present, all the gelatin is digested off within an hour. In cases of meconium ileus nothing will happen apart from a little softening of the emulsion."

Farber's test (in intestinal atresias) consists of the microscopic examination of meconium. If the obstruction has been present for months before birth, no stratified epithelial cells can be seen. These would normally be swallowed *in utero* from the amniotic fluid.

The paper ends with 18 case reports. There are five diagrams and ten roentgenographic reproductions illustrating cases.—*Stanley M. Rogoff, M.D.*

WANSBROUGH, R. M., and CRAM, R. W. Intussusception. *Canad. M.A.J.*, Oct., 1952, *67*, 307–310.

The authors report a statistical study covering 575 cases of intussusception treated at the Hospital for Sick Children in Toronto. This study extends from 1915 to 1950. Sixty-one per cent of the patients were between three months and one year of age, 30 per cent from one year to six years of age, and a few cases were seen in children up to fourteen years of age. The youngest was four days of age. The authors stress the fact that intussusception is extremely rare (1.2 per cent) in children under three months of age.

One hundred and five of the reported cases were operated upon within the first twenty-four hours and there were no deaths. The mortality figures showed a steady increase parallel with the duration of symptoms.

The incidence of different types of intussusception was given as follows: 67 per cent, ileocecal; 17.8 per cent, ileocolic; 6.9 per cent, ileal; 1.6 per cent, colic; 4.7 per cent, compound. Less than 1 per cent were multiple. There were 10 cases of recurrence of intussusception following operation. Recurrence may be associated with Meckel's diverticulum or bowel tumor not removed at the first operation. All the recurrences were late, being weeks or months after the original operation.

Reduction without operation was accomplished in only 12 cases. Four of these were reduced with diagnostic enemas while 8 evidently reduced spontaneously. Meckels diverticulum was recorded in 25 cases, and in most of these cases the diverticulum formed the apex of the intussusception, usually being ileo-ileal or ileocolic.

The over-all mortality rate from 1915 to 1929 was 27.5 per cent, while between 1940 and 1950 it has been reduced to 5.2 per cent. The mortality rate in cases requiring resection was over 80 per cent in the early period and has now been reduced to 23.5 per cent.

This is an excellent presentation and statistical study.—*C. L. Hinkel, M.D.*

LAWRENCE, GEORGE HUGH, and ULFELDER, HOWARD. Intussusception; a review of experience at the Massachusetts General Hospital, 1937–1951. *New England J. Med.*, Oct., 2, 1952, *247*, 499–502.

The authors report on 53 patients treated at the Massachusetts General Hospital from 1937–1951. There were 38 children and 15 adults. It is pointed out that intestinal obstruction is often a late manifestation. Only barium enema was diagnostic. Since in adults the intussusception is commonly in the small intestine, a negative barium enema does not rule out the condition.

In 5 children and 13 adults resection had to be performed because of irreducibility, gangrene, or tumor. Ordinarily the cases are treated surgically and in uncomplicated cases an appendectomy is routinely done.—*C. L. Hinkel. M.D.*

## GYNECOLOGY AND OBSTETRICS

KLEMPNER, EMANUEL, Gynecological lesions and ureterohydronephrosis. *Am. J. Obst. & Gynec.*, Dec., 1952, *64*, 1232–1241.

A group of 218 gynecological patients presenting various lesions of the pelvic organs are presented to determine the relationship between gynecological conditions and ureterohydronephrosis. The frequency of occurrence of urinary tract dilatation with prolapse, cystocele, tumors of the uterus and ovaries, and pelvic inflammatory disease is noted.

The importance of prompt treatment of the conditions is emphasized.

Prolapse of the uterus produced ureterohydronephrosis in 25 per cent. The incidence and severity of urinary tract dilatation increased with the degree of prolapse but cystocele without uterine prolapse did not appear to be a significant factor. Fibromyomas of the uterus produced ureterohydronephrosis in 45 per cent and benign neoplasms of the ovary in 32 per cent, while malignant lesions of the ovary caused dilatation in over 58 per cent.

Carcinoma of the cervix with parametrial involvement caused hydronephrosis in 70 per cent of cases, whereas carcinoma of the fundus caused urinary tract dilatation in 40 per cent. Pelvic inflammatory diseases and endometriosis caused urinary tract dilatation in more than 40 per cent of the patients studied.

Twelve cases manifesting urinary tract infection or impairment of renal function are summarized. Regression of ureterohydronephrosis following correction of benign gynecological lesions occurred promptly in 75 per cent of patients. In cases of pelvic inflammatory disease regression was slower and occurred in only 40 per cent of cases.—*Eugene J. McDonald, M.D.*

Rogers, Wayne S., Gordon, Robert E., and Marsh, Memoir R. The incidence of malignancy in theca-cell tumors. *Am. J. Obst. & Gynec.*, Dec., 1952, *64*, 1289–1295.

Theca-cell tumors are usually benign but the incidence of malignancy cannot be definitely established. Hyperestrinism is usually found in the presence of thecomas. The absence of both atypical bleeding and hyperplasia of the endometrium is not unusual.

There are an insufficient number of thecomas to evaluate properly the correct method of therapy. At the present time, however, surgical removal is the method of choice. In young women the tumor can probably be removed with preservation of the other pelvic organs. In the older patient, panhysterectomy is advisable because of the increased incidence of endometrial carcinoma associated with feminizing mesenchymomas, as well as the malignant potentialities of the tumor. Little is known about the radiosensitivity of these tumors. The experimentally produced tumors in the mouse are radioresistant. Postoperative irradiation is advised in the treatment of malignant thecomas.

One case of malignant thecoma is presented. Five previously reported cases are reviewed but only 3 of these have criteria acceptable for malignant tumors. The incidence of malignancy in theca-cell tumors is approximately 3 per cent.

There is an excellent review of the literature, and photomicrographs of the one case prompting the article are presented.—*Eugene J. McDonald, M.D.*

## Genitourinary System

Bors, Ernest, and Comarr, A. Estin. Vesico-ureteral reflux in paraplegic patients. *J. Urol.*, Oct., 1952, *68*, 691–698.

This study consists of a series of 238 cases selected at random, all of whom had lesions of the spinal cord. In 56 of these patients, evidence of reflux from the bladder to the ureters was demonstrable. The authors used routine cystometry and sphincterometry and, in addition, roentgen examination of the bladder using 70 per cent sterile skiodan solution.

The roentgen technique consisted of serial cystograms made after consecutive 50 cc. amounts of skiodan solution were injected up to a total volume of 400 cc. The alternate films were exposed during the straining phase of the bladder. Among the 56 patients who had reflux, 19 showed demonstrable dye reflux into the right ureter and 12 into the left ureter. In 25 patients, there was a bilateral reflux. Total bladder capacity ranged from 50 to 400 cc. The intravesical pressure with reflux ranged from 0 to 25 mm. of mercury. In 14 instances the reflux was noted on the straining films.

The authors have also correlated reflux and bladder capacity, reflux and detrusor tone, reflux and level of the neurological vision, reflux and the appearance of the ureteral orifice, and reflux and the appearance of the vesical neck. It is interesting to note that reflux at a low volume of 50 cc. was observed almost twice as frequently with small than with large bladders. Extrinsic pressure produced by strain is believed to be an indirect cause of reflux with upper motor neuron lesions and a direct cause of reflux when the patient has a lower motor neuron lesion. No causative relation could be detected between the opening of the vesical neck and the apearance of the reflux.—*George W. Chamberlin, M.D.*

Hutch, John A. Vesico-ureteral reflux in the paraplegic: cause and correction. *J. Urol.*, Aug., 1952, *68*, 457–467.

The author notes the rather high incidence of vesico-ureteral reflux in paraplegic patients. That this reflux is damaging to renal function is illustrated by the fact that of the 14 patients in the paraplegic group whose death was due to urologic disease, 9 had reflux and its complications. The most severe damage to renal function was seen after the third year of paraplegic existence and it was at this time that there was an associated sharp increase in the incidence of vesico-ureteral reflux.

The author describes the anatomy and function of the intramural and intravesical portion of the ureter. He notes that the ureter is firmly attached to the trigone and there is a long intravesical ureter beneath which lies a firm detrusor muscle. This arrangement tends to prevent reflux of urine into the lower ureters.

In 60 of the 94 cystograms which showed reflux of ureters, there was a small out-pouching or diverticulum in the region of the uretero-vesical junction. The consistent association of this defect with the ureteral reflux suggested to the author a possible mechanism. Thirty patients were examined cystoscopically and a definite saccule about the ureteral orifice was demonstrated in 15 instances. These saccules were above and lateral to the ureteral orifice. They involved the bladder wall just beyond the lateral points of the trigone. When a ureteral catheter was passed it would outline the ureter passing under the floor of the saccule. This saccule involved the detrusor muscle so that there was no longer any firm muscle tissue lying under the intramural portion of the ureter.

On the basis of these findings, the authors devised an operation by which the abnormal ureter could be re-inserted into the bladder so that there was a lond intravesical portion. This operation was performed on 9 patients with the elimination of vesico-ureteral reflux in seven.—*George W. Chamberlin, M.D.*

COUVELAIRE, R., MAGDER, E., DEBRAY, J.-R., and GROS-DECAM, A. Documents sur les sténoses de l'uretère du tuberculeux; incidences radiologiques et thérapeutiques. (Ureteral stenoses of the tuberculous; radiological and therapeutic considerations.) *J. d'urol.*, 1952, *58*, 612–657.

The secondary effects of a primary focus of tuberculosis of the kidney on the entire excretory tract (from the calyces to the external urethral metaus) are of great importance in determining the mode and result of treatment. It is not enough to extirpate the primary focus when there is already involvement of the ureter on the normal side. The urinary tract may be involved from within its walls or from without. Parietal tuberculous infection of the ureter will cause stricture if untreated. Submucous, superficial foci do respond favorably to streptomycin and stenosis is often averted. The roentgenological signs of a tuberculous ureteritis are irregularity of the mucosal pattern and fine, yet irregular, indentations of the contour of the involved segment. Deeper foci do not respond to streptomycin and gradually enlarge, caseate and cause stenosis. Sometimes calcium deposits within the borders of caseation can be discovered. Nontuberculous ureteritis can also cause a stensosis and should be investigated before instituting any treatment. Ureteral catheterization and the often observed ensuing traumatic swelling may cause stenotic symptoms and signs.

External encroachment upon the ureters from the psoas and vertebral tuberculous abscesses often causes stenoses. The authors have noted 2 cases in which after nephrectomy, perinephritic tuberculous abscess produced stenosis of the ureter on the normal side at the pyeloureteric junction. The distal end of the ureter is also prone to tuberculous involvement from the genital organs, particularly in the male. Indentation in the contour of the urinary bladder should suggest strongly such an involvement. The sites of frequent stenosis are the ureteropelvic and ureterocystic junctions as well as the intracystic portion of the ureter. There is always some dilatation of the ureter above the level of the stenosis.

Simple roentgenograms of the abdomen and pelvis are of value in demonstrating calcifications in tuberculous ureteritis and sometimes ureteral calculi above the level of the stenosis. The authors believe that a careful intravenous urography is of more diagnostic value than the retrograde urography. Considerable caution should be used in case of retrograde urography because of the danger of traumatic reaction to the ureters and indirectly to the kidneys especially on the affected side. This latter procedure has its advantages from a diagnostic point of view.—*J. N. Sarian, M.D.*

HUGHES, JACK. Ureteral obstruction secondary to extra-ureteral infection. *South. M. J.*, Nov., 1952, *45*, 1044–1049.

The author points out in his opening paragraph that extra-ureteral processes causing ureteral obstruction may be overlooked as the primary condition. This is especially true when the patient's main symptoms are referable only to the urinary tract.

The anatomy of the ureter should be borne in mind. The pelvic part of the ureter is located very close to the sigmoid colon on the left and to the terminal ileum and appendix on the right. In the female, the ureter is very close to the cervix uteri, and also very close to and behind the ovary and fallopian tube. The pathology of obstruction of the ureter secondary to the extra-ureteral infection is rather characteristic. Early findings consist of edema and infiltration with round cells and polymorphonuclears; the result may be dense scarring of the ureteral wall. The author notes that complete roentgenologic study usually establishes the point of obstruction and degree of obstruction. This alone, however, does not make the diagnosis and he stresses careful bimanual vaginal examination of the female and rectal examination in the male. Several cases are presented to illustrate ureteral obstruction with hydronephrosis. Two of these are cases of appendicitis with secondary inflammatory obstruction of the ureter.—*R. E. Kinzer, M.D.*

AURIG, G., and SÜSSE, H. J. Über neue Behandlungsmöglichkeiten der Induratio penis plastica. (New therapeutic possibilities in plastic penile induration.) *Strahlentherapie*, 1952, *89*, 433–436.

The 4 cases reported showed no response to radiation therapy but improved unmistakably under

treatment with vitamin E by mouth. A 50 mg. tablet of synthetic preparation was administered by mouth four times a day for several months so that total dosage varied from 9–29 grams of alpha-tocopherol.

The authors offer these additional considerations: Radiation therapy might be well advised after treatment with vitamin E when the indurated plaques are presumedly more vascular. Dupuytren's contracture, keloids, and even ankylosing spondylitis may consist of the same abnormal reaction of connective tissue as plastic penile induration; treatment of these conditions with vitamin E may be worth while.—*Henry G. Moehring, M.D.*

## Skeletal System

Coventry, Mark B., and Johnson, Einer W., Jr. Congenital absence of the fibula. *J. Bone & Joint Surg.*, Oct., 1952, *34-A*, 941–956.

The fibula, of all the long bones, is the one most commonly congenitally absent. Congenital absence of the tibia, the ulna, the radius and the femur follow in order of frequency. The classical syndrome is one of complete or almost complete absence of the fibula, anterior bowing of the distal third of the tibia with a dimple in the skin at the point of greatest angulation, marked talipes equinovalgus, absence of one or more bones of the foot, and absence of one or more, or fusion of two or more tarsal bones.

In order to determine the best general plan of treatment as well as to determine the prognosis when this treatment is employed, the authors divided the cases of their series into three main types. In the first, the patients have partial, unilateral absence of the fibula with little or no bowing of the tibia. The extremity is always shortened and there is little or no deformity of the foot. In the second type the fibula is completely or almost completely absent. The prognosis for function and appearance is relatively poor, whereas in the first type the only treatment required is a heel lift on the affected side or epiphyseal arrest on the normal side. In type 3, the cases consisted of those showing congenital absence of the fibula of type 1 or 2 associated with other congenital deformities and bilateral absence of the fibula. In this type the absence of the fibula must be accompanied by other congenital defects or it must be bilateral. The condition in most cases is difficult to correct and the prognosis for adequate function is poorer than in the patients of the other two types.

In the differential diagnosis, congenital absence of the tibia must be considered. In the gross appearance there are three important points of difference: (1) The foot and ankle in congenital absence of the tibia are in a varus position, not in valgus. The medial malleolus is missing, with resulting medial displacement of the ankle. (2) While atrophy and shortening of the leg are present, as in congenital absence of the fibula, there is little or no anterior bowing of the leg. (3) There is dislocation of the knee. Without the normal articulation of the tibia on the femur, the fibula rides laterally and there is no true knee joint. Roentgenographically, it is sometimes difficult to distinguish between the tibia and fibula.

The gross appearance of the leg in cases of congenital pseudarthrosis of the tibia is often similar to that in cases of congenital absence of the fibula. In roentgenograms of congenital pseudarthrosis of the tibia, the tibia and fibula are thickened and may be angulated or fractured. The fibula is always present except at the site of the pseudarthrosis. Other conditions to be differentiated are congenital equinovalgus, posteromedial bowing of the tibia and fibula.

The authors recommend treatment of the deformity in congenital absence of the fibula as soon after birth as possible. Partial correction in casts is the first procedure and the correction is held until walking age when a prosthesis can be made. The child walks in this until the age of two or three years, at which time operative procedures can be performed, including posterior and lateral section of soft tissues and osteotomy of the tibia. A prosthesis is worn until bone growth is completed. Thereafter the lateral malleolus can be grafted if necessary to help hold the calcaneus and talus in position.

The authors report that many patients get good functional results from this form of treatment. They state that amputation should not be performed in cases of bilateral absence of the fibula. In cases of unilateral absence, it usually should not be done until maturity has been reached. If at that time amputation is indicated for functional and cosmetic reasons, it may be performed.—*Ralph S. Bromer, M.D.*

Anderson, Kirk, J., Lecocq, John F., and Lecocq, Edward A. Recurrent anterior subluxation of the ankle joint: a report of two cases and an experimental study. *J. Bone & Joint Surg.*, Oct., 1952, *34-A*, 853–860.

Two cases of anterior subluxation of the ankle joint are reported in this paper. They demonstrate appreciable subluxation of the talus in the coronal plane only. Recurrent subluxation of the ankle joint has been established as an entity in the last two decades and roentgenographic examination of the ankle joint under inversion strain is now regarded as an absolute necessity for accurate diagnosis in such cases. Tilting or lack of parallelism of the articular surface of the talus in relation to that of the tibia is indicative of recurrent subluxation.

Accurate diagnosis depends largely upon on the roentgenographic examination of the ankle joint under strain, with or without anesthesia. Because of the relative thinness of the anterior talofibular ligament, a complete rupture of this structure may occur, with a force which would produce only a minor

sprain of a stronger ligament such as the calcaneofibular ligament. The 2 cases reported in this paper had isolated ruptures of the anterior fibular ligament with absence of tilting in one and only a slight degree of tilting in the other. Lack of response of both patients to conservative measures necessitatesd surgical repair, although most authors in reported cases state that such an isolated rupture is unimportant.

Experimental observations were made on 2 fresh and 5 preserved specimens to assess the importance of the various components of the lateral ligament in maintaining stability of the ankle joint in the coronal plane. The anatomy of the lateral ligament is described and the experimental observations are given in detail. One practical point mentioned is that, in the presence of a rupture of the anterior fibular ligament, the lateral capsule, lateral talocalcaneal ligament and calcaneofibular ligament are torn with little additional inversion force, and caution is suggested against forcible manipulation of the ankle under anesthesia for diagnostic purposes.—*Ralph S. Bromer, M.D.*

NACHLAS, I. WILLIAM. End-result study of the treatment of herniated nucleus pulposus by excision with fusion and without fusion. *J. Bone & Joint Surg.*, Oct., 1952, *34-A*, 981–988.

This article is the report of the chairman of the Research Committee of the American Orthopedic Association on the investigation of the treatment of herniated nucleus pulposus by excision with fusion and without fusion.

From the material analyzed in this study, the committee concluded that it would seem that, if 100 patients with herniated nucleus pulposus are subjected to disc incision, one may expect 60 of them to obtain long-term results which are satisfactory. If the same 100 patients should have spine fusions in addition to the disc excisions, the results will be satisfactory in 70 of them. Sixty of these patients would not have needed the fusion operation, and the 40 whose results are unsatisfactory only 10 could have expected sufficient improvement to make them satisfactory. Furthermore, the fusion procedure is an added operation, and the committee believes that there is no reason to feel that its effectiveness is greater if it is done at the time of the disc excision than if it is performed at a later date as a second-stage operation. The committee is therefore led to the conclusion that, when surgical intervention is necessary for simple cases of herniated nucleus pulposus, the operation of choice is disc excision only. Spine fusion can be performed at a later date in those patients whose poor results warrant additional surgery.

The committee also recognized the fact that technical improvement in the operative procedures may be expected. Such improvement may lead to results which differ from those found in this study and will justify a re-evaluation after a lapse of years.—*Ralph S. Bromer, M.D.*

DREWES, H. G. Intraossäre Geschosswanderung. (Intraosseous migration of a projectile.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Oct., 1952, *77*, 451–455.

An infantry projectile, which had become lodged in the distal end of the femur, was observed roentgenographically at various intervals for a period of thirty-seven years and finally presented as a loose body within the joint space of the knee. The author believes that gravity played the major role in the process of wandering, but he also postulates a cellular activity occasioned by an alteration of the osteoblast-osteoclast equilibrium of the bone at the site of the aseptic wound.—*Joseph Zausner, M.D.*

ZELLWEGER, H., GIACCAI, L., and FIRZLI, S. Gargoylism and Morquio's disease. *A.M.A. Am. J. Dis. Child.*, Oct., 1952, *84*, 421–435.

This paper, according to the authors, is concerned with the difficulties in the differential diagnosis of abortive and late forms of gargoylism. They state that the fully developed picture of gargoylism is characterized by the following groups of symptoms: (A) Epimetaphyseal dysostosis or dysostosis-dysdesmosis syndrome: short growth; stunted trunk, with lumbar kyphosis and deformities of the sternal bone; short and sometimes distorted extremities; short, broad, and stubby fingers; large, sometimes scaphocephalic skull, with a prominent forehead and bulging parietal bones, and reduced mobility of the articulations (claw hands), or, in other cases, increased mobility of the joints. (B) Signs of lipid or, according to Lindsay, glucoprotein storage: hepatosplenomegaly; cloudiness of the corneas; progressive mental deterioration; abnormal granulations in the white cells and the bone marrow. (C) Accessory signs: gruesome gargoyle face, hypertrichosis; flabby skin; umbilical hernia; tendency toward frequent upper respiratory infections, etc.

When all these signs are present, it is easy to recognize a case of gargoylism. However, there exist a number of cases in which there are only traces of the storage syndrome. Whether in the late form of Hurler's disease the lipid or glucoprotein storage is confined to the corneas, or whether later splenomegaly and cerebral symptoms will occur, is at present unknown. There are, however, cases in which the skeletal disturbances can be noticed early, whereas the storage symptoms appear later.

The authors quote Caffey, stating that in the earliest phase of gargoylism, in early infancy, the roentgenological bone changes are different from those in the later phase, since there are generalized rarefaction and metaphyseal spreading, cupping and spurring

which are suggestive of rickets or hyperparathyroidism. They give the following differentiating roentgenological signs of Morquio's disease and gargoylism: in the skull the sella turcica in Morquio's disease is normal whereas in gargoylism it is enlarged, with a shoe form; in the vertebral bodies platyspondyly with irregular epiphyseal plates is found in Morquio's disease, while in gargoylism the vertebral bodies have a beak-like protrusion of anterior edge, especially marked in the second and third lumbar vertebrae; in Morquio's disease the long bones have normal diaphyses, but in gargoylism they have enlarged diaphyses tapering toward the metaphyses; in Morquio's disease the epiphyses are small, irregular, ill-defined and fragmented, but in gargoylism they are bigger than in Morquio's disease; normal or delayed bone maturation is found in the carpal ossification centers in Morquio's disease whereas in gargoylism there is delayed maturation; in Morquio's disease the ribs are normal, in gargoylism they are of a spatulated or oar form.

Three cases are presented in the paper. In the first case, the patient's skeletal changes were well developed by the age of five years but the signs of storage disease could not be seen at this age and did not appear until later. At the age of nine, the full picture of gargoylism developed.

In the second and third cases, the patients were siblings of a consanguineous family. The second case was a nine year old child with a fully developed gargoylism, the third was two and a half years old and had typical skeletal changes but, as far as the storage syndrome was concerned, only small deposits in one cornea and abnormal granules in the leukocytes were found.

The authors think that clouding of the corneas and granulation anomalies in the leukocytes and/or lymphocytes may appear earlier than the hepatomegaly and signs of brain involvement. They therefore suggest that in every case of suspected gargoylism corneal changes should be searched for with the slit lamp and the white blood cells be examined for abnormal granules in order not to overlook the diagnosis of the condition in an early stage.

In none of the 3 cases were the roentgenological signs described as characteristic for Hurler's disease fully represented, In the first case the changes were similar to those of the pleonostosis described by Léri. In the second and third cases some of the characteristic signs were present but in each case the sella turcica was normal. Some long bones showed tapering of their ends but others showed wide flaring of the metaphyses. The authors therefore believe that, in most cases, a differential diagnosis between the types of epimetaphyseal dysostosis based only on roentgenological changes is unreliable.—*Ralph S. Bromer, M.D.*

Whiteside, J. D., and Cholmeley, J. A. Morquio's disease; a review of the literature with a description of four cases. *Arch. Dis. Childhood*, Oct., 1952, *27*, 487–497.

The authors present a review of the literature and a description of 4 cases of Morquio's disease which occurred in a family with eight children. The family displayed two hereditary disorders: (1) Morquio's disease in the fourth, fifth, seventh and eighth children, and (2) mental defect, dolichocephaly, and abnormally long palate and possibly a scoliosis in the first, fifth and eighth children, the fifth and eighth children having both groups of abnormalities. The authors believe this is a hereditary disease transmitted as a recessive.

Morquio described the essential features of the disease for the first time and recognized the condition as a hereditary dystrophy of cartilage and bone resulting in dwarfism and generalized skeletal deformity. The following findings were noted: marked spinal kyphosis with angulation at the dorsolumbar region; chest deformity with increased anteroposterior diameter and the sternum thrust forward horizontally to a point; raised clavicles and a short neck, giving an appearance as if the head were thrust into the deformed thorax; genu valgum from enlargement of the internal femoral condyles; large flat feet with varus deformities; enlargement of the head and epitrochlear of the humerus; feeling of emptiness in the wrist joint and excessive range of movement. Morquio stressed the lax ligaments and low muscle tone, the grating and crepitation in the joints, the difficulty in locomotion, the irregularity, deformity and delayed ossification in the epiphyses. In his earlier 2 cases there was a lowered serum calcium level, not present in the later cases. Other biochemical findings were normal. The pelves and hips were not affected in his cases.

Brailsford reported on the roentgenological changes in detail. He emphasized the irregularity and fragmentation of the epiphyses, the multiple centers of ossification, the large joint spaces, the short, thick long bones with coarse, irregular reticulation of the cancellous tissue and absence of regular lines in the lamellae. He described the wide flat vertebral bodies (platyspondia), some pointed in front and some wedged-shaped, the wide intervertebral discs, the erosion of the acetabula and heads of the femora, the irregularity of the carpal and tarsal bones, and the pointed bases to the metacarpals and metatarsals. He attributed the prominent thorax to arrest of growth of the spine at the cervicodorsal junction.

The biochemical findings have shown normal serum calcium levels in the majority of the cases. The inorganic phosphate levels were normal. Some authors have stressed a raised basal metabolic rate and lowered blood cholesterol.

This study comprises all phases of the disease but fails to add anything further to the etiology or treatment of the condition.—*James F. Martin, M.D.*

HALL, RICHARD H., and MENDELOFF, JOSEPH. Blastomycotic osteomyelitis; with a case report. *J. Bone & Joint Surg.*, Oct., 1952, *34-A*, 977–980.

A case of blastomycosis is reported in a white male, aged twenty-one. The roentgenographic findings were marked osteoporosis of the tarsal bones of the right foot. The second and third cuneiforms were not discernible and apparently had been destroyed. Marked sclerosis of the talus and calcaneus was present. The proximal ends of the second and third metatarsals were partially destroyed. Pulmonary findings on admission were reported as negative. Roentgenograms of the skeleton showed no additional lesions. The skin test with blastomycin vaccine was positive and *Blastomyces dermatitides* was identified from growths recovered from the blood agar plates and Sabouraud's medium. The lesion ultimately healed and the patient could walk for long distances without a limp, and could stand indefinitely without symptosm.

The authors review the literature briefly and in their conclusion state that the prognosis for osteomyelitis due to this type of blastomycosis is not necessarily poor and it depends on the degree of dissemination. They stress the kinship between blastomyelitis and tuberculous osteomyelitis in pathogenesis, differential diagnosis and treatment. Surgically it is possible to remove foci of infection at times and thus prevent further dissemination. However, they feel that each case should be carefully studied from all aspects and that, as a general rule, surgery should be more conservative than in tuberculosis.—*Ralph S. Bromer, M.D.*

JOHNSON, MAURINE, P., and ROTHSTEIN, EMIL. Tuberculosis of the rib. *J. Bone & Joint Surg.*, Oct., 1952, *34-A*, 878–882.

Three cases are reported of tuberculous involvement of the posterior portion of a rib. Tuberculosis of the rib is a rare condition. A distinction must be made between tuberculous chondritis, involving the costal cartilage, and tuberculous osteitis, involving the body of a rib at a distance from the cartilage. Tuberculosis of the costal cartilage is much more common and may result in the formation of abscesses and sinuses, as well as in the infection of the adjacent bone. Isolated hematogenous, tuberculous osteitis of the rib, particularly in the posterior portion, the authors state, has been reported infrequently.

In the 3 cases described, an osteolytic process alone was observed in the roentgenograms. There was no evidence of periosteal activity, sequestration, or calcification. This was due possibly to the early resection, as in tuberculous involvement of other bones, soft tissue calcification and bone regeneration was observed with prolonged conservative treatment.

Tuberculosis of the rib must be distinguished from other types of inflammatory bone lesions of the ribs and from benign and malignant tumors. Cold abscesses, when present, must be distinguished from cysts and tumors of the chest wall and from the somewhat more common type of cold abscess in this area secondary to tuberculosis of the thoracic spine. The lateral location of the abscess, the results of aspiration, and the use of repeated roentgenograms of the underlying ribs will enable a differential diagnosis to be made.

The treatment employed in the 3 cases consisted of incision and drainage of the abscesses found at operation with resection of the involved bone after a short interval. Streptomycin was used alone in 1 of the cases and with para-aminosalicylic acid in the other 2 cases.—*Ralph S. Bromer, M.D.*

WAGNER, CARRUTH J. Fractures of the carpal navicular. *J. Bone & Joint Surg.*, Oct., 1952, *34-A*, 774–784.

This paper is based on the results obtained in the treatment of aseptic necrosis of the proximal fragment in fractures of the carpal navicular. Thirty-seven cases were followed and end results were compared. With early recognition, reduction of displacement, and uninterrupted immobilization of the wrist in dorsiflexion, union will almost invariably occur in a reasonable length of time with little or no disability. All of the fractures of the series represented fractures of the waist or of the proximal pole of the bone. The diagnosis of aseptic necrosis was based upon the roentgenographic evidence of failure of the proximal fragment to de-ossify with immobilization. In cases in which the fragment was removed the diagnosis was confirmed by pathological examination.

Three methods of treatment were used in this study: prolonged immobilization, removal of the avascular fragment, and removal of the entire navicular.

In comparing his results of the series of cases, the author states it would appear that the best results were obtained with immobilization until revascularization of the proximal fragment has occurred. When such a method of treatment is unacceptable, fairly satisfactory results can be obtained with excision of the proximal fragment. Definite changes, however, occur in the carpus as a result of the loss of the proximal fragment. The follow-up period of his cases was too short to determine whether these changes result in significant disabilities later in life. He suggests that this procedure could be reserved for the older age group and that the younger patients be encouraged to undergo the prolonged immobilization.

Five cases of total excision were not satisfactory in their end results and Wagner finds little indication for this procedure.

In removal of the proximal fragment, he does not regard the rounding off of the distal fragment or excision of the radial styloid as necessary for a good result.—*Ralph S. Bromer, M.D.*

Garsche, R. Über den Verlauf der sog. akuten, hämatogenen Osteomyelitis im Säuglingsalter unter Penicillin. (The effect of penicillin on the course of acute, hematogenous osteomyelitis in infants.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver m. Röntgenpraxis*, Oct., 1952, *77*, 395–408.

Osteomyelitis is divided into three stages: metaphysitis, subperiosteal reaction, and medullary abscess. While abortive forms were not rare prior to the penicillin era, they have become more frequent since the advent of antibiotics. Furthermore, they have brought abscesses to quicker resolution and the periosteal reactions subside sooner. Osteomyelitis in infants may not be roentgenographically recognizable for eight to fourteen days after clinical onset of the disease. This "negative phase" may be diagnosed earlier, however, by careful examination for osteoporotic changes characterized by blurring of the trabeculations, slight periosteal elevations, and a feathery appearance of the muscle bundles adjacent to the involved site.

Penicillin has decreased the mortality of infants with osteomyelitis, but often the recovery phase has been prolonged. The earlier the administration of the antiobiotics, the better are the chances for a recovery with a normal size and function of the involved part.—*Joseph Zausner, M.D.*

Etter, Lewis E. Detailed roentgen anatomy of the orbits. *Radiology*, Oct., 1952, *59*, 489–503.

The author reviews the bony anatomy of the orbits. By means of many excellent roentgenographic reproductions and drawings of various sections of bone comprising the orbits, he demonstrates the structures which represent various previous confused shadows about and within the orbits.

It is suggested that those interested in the subject refer to the original article for special study of the reproductions.—*Everett E. Seedorf, M.D.*

Odena, Isidro Castillo. Bipolar fracture-dislocation of the forearm. *J. Bone & Joint Surg.*, Oct., *1952*, *34-A*, 968–976.

Bipolar fracture-dislocation of the forearm is a rare injury which consists of fracture of the proximal third of the ulna with dislocation of the head of the radius and simultaneous fracture of the distal third of the radius with dislocation of the distal extremity of the ulna. The author states that it might be described as a concomitant Monteggia and Galeazzi fracture. Galeazzi fracture consists of a fracture of the radial shaft 8 cm. above the wrist joint combined with a dislocation of the distal extremity of the ulna.

The author observed 3 patients, 2 of whom he was able to follow. He believes that bipolar fracture-dislocation of the forearm is an injury associated with modern transportation. It results from two opposing forces acting on the forearm. The patient is usually seated in a vehicle with the elbow flexed to a right angle, resting on the window ledge and projecting through the window with the hand pronated and in hyperextension on the hand rest. When the passing vehicle "sideswipes" the car in which the man is sitting, the elbow is struck from behind and is forcibly impacted against the hand, which is firmly held in pronation. The opposing forces act in a manner similar to that which has been described for Monteggia's fracture.

Debridement is recommended as the correct treatment for this fracture-dislocation which is usually compound. Thereafter he recommends that the lower end of the ulna should be resected to facilitate a closed reduction of the Monteggia fracture. The dislocation of the head of the radius can be reduced by supinating the forearm and applying pressure over the radial head. If satisfactory union of the fractures in the ulna and radius occurs, good flexion-extension of the elbow and pronation-supination of the forearm will be obtained.

The paper is illustrated with roentgenograms of the injury and diagrams illustrating the mechanism of the fracture.—*Ralph S. Bromer, M.D.*

Macnab, Ian. Recurrent dislocation of the patella. *J. Bone & Joint Surg.*, Oct., *34-A*, 957–967.

This paper is a study of 64 cases of recurrent dislocation of the patella in 46 patients. The condition was bilateral in 18 and unilateral in 28. Six were males and 40 females, and the average age at the time of first dislocation in both males and females was thirteen years, with a range of six to twenty-one years in the males and three to twenty years in the females.

By combining a study of the roentgenograms with the pathological changes presented, it was possible to recognize a progressive degeneration of the patello-femoral joint. The degenerative changes which were seen fell into five groups:

Group I. In the first group the roentgenographic findings were within normal limits and the degenerative changes were demonstrated only at operation. The earliest changes were confined to the patella, and the first stage seemed to be a fibrillation and heaping up of articular cartilage on the medial facet. As this degeneration progressed, a small crater with soft fibrillated cartilage heaped up around its mouth appeared on the medial side of the patella.

Group II. Roentgenograms of the knee showed evidence of degeneration. There was damage on the medial facet of the patella and a small loose body was sometimes seen in relation to the medial edge. The changes in the cartilage were similar to those seen in the first group but slightly more severe.

Group III. Roentgenograms of the knee showed

degenerative changes in both the patella and the femur, and pathologically the subchondral bone, as well as the cartilage, showed evidence of damage. More and more cartilage of the patella had been worn away and the underlying bone had become eburnated, exposed and planed off. In this group the lateral roentgenograms of the knee frequently showed a spur of bone heaped up at the upper border of the patellar surface of the femur.

Group IV. In this group there was frank patellofemoral osteoarthritis. The patella had lost its median ridge and its femoral surface was planed off.

Group V. In the fifth group, there was generalized osteoarthritis of the knee joint. This change was found in all patients with untreated recurrent dislocation of the patella of more than thirty years' standing.

Eight different operative procedures were used. Because of the small number of patients in the series, it was not possible to assess the merits of each technique. In the over-all results those in the series with a short follow-up period were encouraging. The long-term results, however, did not present such a satisfactory picture. All patients had clinical or roentgenographic evidence of osteoarthritis and were handicapped in their activities to a varying extent.

As the routine anteroposterior and lateral roentgenograms reveal only the gross changes in the articular surface of the patellofemoral joint, the most information can be gained with the use of the so-called "sky-line" projection. The patient lies face downward on the table with the cassette under the fully flexed knee. Damage to the medial facet of the patella and loose bodies in this region can be demonstrated by this method.

The small series would seem to show that almost any operative technique, adequately performed, will prevent redislocation and give good early results. The long-term results were found to be disappointing. It is felt by the author that surgical intervention should be undertaken early in the hope that movement of the patella can be restored to normal before articular cartilage is destroyed. As it is impossible to assess accurately the degree and extent of articular degeneration by clinical means it is suggested that the knee joint be opened and inspected in patients on whom operation is performed and, if there is marked damage, the patella should be excised, and the pull of the quadriceps be realigned. Probably the easiest way of realigning the pull of the quadriceps is to transplant the tibial tubercle medially. This operation has been successful in adults but has certain hazards when performed in children. If the severe damage to the patellar cartilage which frequently occurs is unnoticed or ignored, the patient will probably be condemned to early onset of osteoarthritis of the knee, with a final result as disappointing as that in patients on whom no operation has been performed.—*Ralph S. Bromer, M.D.*

DURAISWAMI, P. K. Experimental causation of congenital skeletal defects and its significance in orthopaedic surgery. *J. Bone & Joint Surg.*, Nov., 1952, *34-B*, 646–698.

This article is a very voluminous report of the author's study of congenital defects, especially with reference to the methods of their causation. He states in his summary that he attempted to review in some detail the more important work which has been carried out on experimental teratogenesis, on the epidemiological implications of developmental arrests in humans, and on fetal abnormalities associated with maternal metabolic and hormonal disorders during pregnancy.

In 1943, the author, while investigating the role of glycogen granules in hypertrophic cartilage cells in chick embryos during endochondral ossification, made an accidental observation as a result of which he became interested in the insulin-induced skeletal abnormalities in developing chick embryos. In his article he describes the technique employed for injection of insulin into the egg-yolk and outlines methods for the estimation of blood sugar in chick embryos at various stages after injection of insulin and special isochemical techniques for localizing polysaccharides in cartilage. Insulin-induced abnormalities can be prevented to a remarkable extent by injecting nicotinamide and riboflavin into eggs along with insulin. The question of the practical application of the knowledge gained from experimental observations on insulin-induced developmental abnormalities in explaining the possible causation of congenital anomalies in humans by genetic and environmental teratogenic factors is discussed. He thinks in regard to the possible prevention of congenital deformities that it is not always easy to offer sound eugenic advice in the cases of congenital malformations determined partly or comgletely by genetic factors.

He thinks that further energetic investigation of the causes of prematurity, stillbirths, monstrosities and congenital malformations is urgently needed before any program for prevention can be instituted.—*R. S. Bromer, M.D.*

CAFFEY, JOHN. On some late skeletal changes in chronic infantile cortical hyperostosis. *Radiology*, Nov., 1952, *59*, 651–657.

Infantile cortical hyperostosis is usually a benign disease with clinical manifestations subsiding after a few weeks and roentgenologic skeletal changes disappearing within a few months. The chronic type of the disease with late crippling skeletal residuals has been rarely reported.

The patient whose case is reported in this paper was studied, clinically and roentgenologically, between the ages of four months and twenty-seven

months, and when last examined was still deformed and disabled by late skeletal changes.

The early changes were external thickening of the cortical walls with a normal-sized medullary cavity. There followed progressive thinning of the cortical walls from the inside, reciprocal dilatation of the medullary cavity, and persistence of the external swelling of the shaft. In this case, reported for the first time in this disorder, there occurred bone bridges between each ulna and radius and between contiguous ribs. Persistent ventral bowing of the tibiae, as reported in other cases, was not found in this instance.—*Lynne J. Taylor, M.D.*

Swoboda, W. Die Röntgensymptomatik der Vitamin-D-Intoxikation im Kindesalter. (The roentgen appearance of vitamin D intoxication in childhood.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Nov., 1952, 77, 534–545.

Thirteen cases showing roentgen changes are discussed.

The three characteristic findings were: (1) abnormal calcium deposits in the skeleton and soft tissues, (2) osteoporosis, and (3) periosteal reaction.

Several transverse bands of increased density were seen in the preparatory zone of calcification of long bones. These must be differentiated from "growth lines," scurvy, phosphorus and heavy metal poisoning. Calcifications in the falx, tentorium, petroclinoid ligaments and diaphragma sellae were not uncommon. Four cases exhibited calcification in the soft tissues on the lateral aspect of the knee joints and were thought to have calcium deposits on the surface of the epiphyseal cartilage of the patella. One case showed calcification in the limbus of the acetabulum. Osteoporosis similar to that seen in lues, sepsis and leukemia was noted in the ends of the diaphysis. The cortex appeared lamellated. Periosteal new bone formation, similar to that seen in pulmonary arthropathy, was present in the metacarpal bones.

While one single sign is insufficient for diagnosis, a combination of them is diagnostic. Congenital or acquired chronic renal insufficiency must be considered in the differential diagnosis.

Roentgenograms of the following areas are recommended for diagnosis: skull, in the anteroposterior and lateral views; both hands and distal ends of forearms, both knees, in the anteroposterior view; and both legs, in the anteroposterior view.

The pathogenesis is discussed in detail.—*Frederick M. Reis, M.D.*

Leb, A. Die Röntgendiagnostik der Periarthrose und der Periarthritis. (The roentgen diagnosis of periarthrosis and periarthritis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Nov., 1952, 77, 525–534.

The following techniques are used to study the soft tissues of joints:

1. Plain roentgenogram for soft tissue detail with a short and slightly overpenetrated exposure and an underdevelopment of the film.

2. Injection of contrast material (30 per cent ioduron) into the periarticular spaces, bursae and parafascial loose connective tissues.

3. Arthrography (30 per cent ioduron) to show the effect on the joint space of periarthritic processes.

4. Serial arteriography to show periarticular ischemia which accompanies shrinking periarticular fibrosis.

5. Resorption tests after injection of water-soluble contrast material into the joint space. This may demonstrate impaired lymph drainage and decreased blood supply in periarthritis. Ioduron normally is absorbed in two hours.

In pathological cases the plain roentgenogram shows unsharpness and irregularity of soft tissue contours, absence of loose soft tissue spaces and increased, homogeneous density of soft tissues.

Serial arteriograms in periarticular fibrosis show poor collateral circulation, the resorption of intra-articular ioduron being slow. However, in acute, hyperemic periarthritic processes it is accelerated.

These techniques are simple and can be used in any roentgenologic department.

In concluding, the author states that much information can be obtained in the study of joint disease by paying detailed attention to the periarticular soft tissues and blood vessels.—*Frederick M. Reis, M.D.*

Jesserer, H. Zum Erscheinungsbild der Akroosteolyse. (The roentgen appearance of acro-osteolysis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Nov., 1952, 77, 545–552.

Three years ago Harnasch described a case of acro-osteolysis expressing the opinion that the disease represented a new entity (see abstract this Journal, 1950, 64, 553–554). The author discusses this case, another case reported in the literature and 2 cases of his own and comes to the following conclusions:

In generalized disturbance of osseous metabolism, such as osteomalacia and primary and secondary hyperparathyroidism, atrophy of the distal phalanges takes place causing clubbing of the fingers and toes. The ungual tufts become mushroom-shaped while the remainder of the phalanx shows extensive osteolytic destruction. The changes are more pronounced in the thumbs and hands than in the toes. Osteolytic changes in the acromioclavicular areas and the disappearance of the lamina dura of the alveolar processes have the same significance.

Since no specific cause could be found in the Harnasch case, the condition cannot be considered a new entity of nervous-endocrine etiology. Eight

cases have been described so far in the literature.—*Frederick M. Reis, M.D.*

TAYLOR, R. G., and WRIGHT, P. R. Posterior dislocation of the shoulder; report of six cases. *J. Bone & Joint Surg.*, Nov., 1952, *34-B*, 624–629.

Six cases of posterior dislocation of the shoulder are described in this paper. In 4 cases the diagnosis was made on clinical grounds, the important clinical signs being the adducted and medially rotated position of the arm, a hard mass posteriorly below the acromion representing the displaced humeral head, and limitation of movement, especially abduction and lateral rotation. In 2 cases the dislocation was not recognized at first examination.

Posterior dislocation of the shoulder is generally the result of direct violence, usually by a blow on the front of the shoulder, or a fall on the hand with the arm flexed and adducted at the shoulder. In 2 of the patients there was a clear history of a direct blow on the shoulder, and in another the degree of bruising of the front of the shoulder suggested the same mechanism. An associated fracture of the head or the greater tuberosity of the humerus was present in 4 patients.

Roentgen examination was inconclusive until the vertical projection was employed. In 2 patients the posterior dislocation was not diagnosed at the first examination and, although the anteroposterior roentgenogram suggested an abnormality of the joint, a vertical view was necessary to confirm the diagnosis.

Most modern methods suggest reduction with traction with adduction, assisted if necessary by direct pressure upon the displaced head. Reduction was accomplished without difficulty in 5 cases and the subsequent progress of these was uneventful. In the remaining case reduction was difficult and unstable, and final recovery was incomplete.—*R. S. Bromer, M.D.*

BILLING, LARS, and GEDDA, K.-O. Roentgen examination of Bennett's fracture. *Acta radiol.*, Dec., 1952, *38*, 471–476.

Bennett's fracture was described in 1882 by the Irish surgeon E. H. Bennett. It is an intra-articular solution of continuity of the base of the metacarpal bone of the thumb. The lower volar extremity with a greater or smaller part of the joint surface forms a fragment which is held in its correct position in relation to the greater multangular by its ligamentous attachment. At the same time, the shaft of the metacarpal bone is displaced more or less dorsoradically by the pull exerted by the musculus abductor pollicis longus.

A Bennett's fracture which heals with deformity may, according to Swedish regulations governing workmen's compensation, constitute a 25 per cent disability (a disability of the same order as a fracture of the femur in poor position).

As a rule, accurate reduction and fixation can be achieved only by operation. This consists of opening the joint from the volar aspect and inserting a Kirschner wire into the small fragment. After the displacement has been corrected the wire is looped through the main body of the bone itself and when healing has occurred, it is removed.

To show the base of the first metacarpal and the joint between it and the greater multangular correctly, a true lateral view is most important. Such a projection may be obtained in the vertical plane if the palmar surface of the hand is placed flat on the film and the hand and wrist then is pronated 15°–35°. If the rotation is insufficient the dorso-radial tubercle on the greater multangular bone will protrude. With the tube displaced distally and the central ray directed at an angle of 20°–30° from the vertical, the ulnar and radial joint margins of the greater multangular are accurately superimposed. In a true lateral view the first carpometacarpal joint is projected over the base of the second metacarpal bone and the greater and lesser multangular bones are superimposed.

A simple apparatus for the fixation of the hand is described. This facilitates positioning and makes it possible to carry out accurate repeat examinations. —*Mary Frances Vastine, M.D.*

SMILLIE, I. S., and MURDOCH, J. H. Man with three legs. *J. Bone & Joint Surg.*, Nov., 1952, *34-B*, 630–635.

The patient whose congenital anomaly is described in this case report was a man, aged fifty, the youngest of six children who were otherwise normal healthy individuals. When the abnormal infant was born, the doctor who was present recommended that the apparent tumor be immediately removed. Treatment, however, was firmly refused. The patient's life had been one of complete seclusion. Until the age of ten he was concealed from view in a perambulator. From that time he was known to have run about freely, wearing a kilt. When the tumor outgrew the kilt, his parents clothed him in a dressing gown. The wearing of trousers was impossible. He came to the hospital for admission for removal of tumor, which was actually a third leg, bandaged to his right leg, with his infirmity concealed by a long skirt.

The third limb took origin from the right side of the midline in the gluteal region. The base, centered 2½ inches from the natal cleft, was 17 inches in circumference. The total length, excluding the lower leg and foot, was 17 inches. The leg encircled the thigh at its distal end and to the leg was attached a con-

pletely inverted foot possessing a well-formed heel and five normal toes with nails. A long slender accessory toe without a nail grew from one side of the first metatarsal. On the anteromedial aspect of the mass, between 5 and 8½ inches from the superior boundary of the base was an area of loose, wrinkled, hair-covered scrotal skin with a raphe from which a penis, with a bifid glans and hypospadias, protruded. No testes were present.

Roentgenograms showed that the base of the limb included a rudimentary pubis and ischium. Articulating with this hemipelvis was a femur which ended distally in bony ankylosis with a malformed curved tibia. Neither patella nor fibula was present. The tarsus was represented by a fused mass of bones. The metatarsals and phalanges were normally formed but with the addition of an accessory first metatarsal.

Roentgenograms of the chest showed a large mass in the anterior mediastinum displacing the heart and trachea to the left. It was later proved that this tumor was a very large intrathoracic goiter arising from the right lobe of the thyroid gland.

The patient was operated upon and the third limb was successfully removed. He was discharged from the hospital but he died three months later at his home. At postmortem, the bladder was found to be full of pus and the mucous membrane, especially of the posterior diverticulum, was acutely inflamed. A scirrhous carcinoma of the prostate invading the base of the bladder was found on section. There was no evidence of an additional urethra, nor of any other embryological abnormality.

The authors include a review of previous reports of somewhat similar cases in the literature. A roentgenogram of the bony structures of the third limb is included in the illustrations.—*R. S. Bromer, M.D.*

Jahss, Melvin. Congenital coxa vara; preliminary clinical followup. *Bull. Hosp. Joint Dis.*, Oct., 1952, *13*, 342–355.

The author reports the clinical and roentgenographic follow up of 16 cases of congenital coxa vara seen over a period of twenty-six years. In 7 cases, or 30 per cent, the condition was bilateral. The right and left hips were equally involved. There were 10 male and 6 female patients.

In the typical case, roentgenograms showed the femoral head was normal in size and shape, but appeared enlarged due to its juxtaposition with the underdeveloped narrow sclerotic neck. The greater trochanter also appeared large and was beaked and curved inward. The femoral shaft was displaced upward. The epiphyseal plate appeared vertical and was bifurcated into an inverted "Y," enclosing a separate triangular island of ossification. Finally, there was a relatively large "mushroom" femoral head and a thin sclerotic neck.

Three cases, including 2 patients with minimal coxa vara, were untreated. While no gross evidence of osteoarthritis was noted the typical limitation of motion, limp, shortening and a positive Trendelenburg sign were present.

The best results in the therapy of congenital coxa vara were obtained in those cases in which subtrochanteric osteotomy alone was performed at an early age. The end result was a practically normal shaped femoral head upon a large stubby femoral neck with a normal greater trochanter. While the ideal age for correction is from five to eight years, operation should not be delayed at any age with s progressive varus deformity, nor past nine years when the femoral neck becomes sclerotic and narrow and the greater trochanter beaked shaped. Roentgen control in the operating room is not only essential in determining the amount of operative correction but also the exact level of the osteotomy.—*J. N. Ané, M.D.*

Sandaa, Eigil. Orthoroentgenographic measurement of long bones. *Acta orthop. Scandinav.*, 1952, *22*, 76–79.

A modification of Goldstein and Dreisinger's "spot orthoroentgenography" is described. The technique and equipment required are simpler, and the need for 14 by 36 inch film is eliminated.

A tunnel is made of 7 mm. plywood, 116 cm. long and 20 cm. wide, with 2 cm. between top and bottom. The sides are left open, two movable crossbars in the tunnel serve as supports, and there is a footrest at one end. A 100 cm. ruler is inlaid longitudinally in the top. There is a radiopaque marking at each cm. and every fifth cm. is marked by radiopaque numerals.

The patient is placed on the tunnel with the longitudinal axes of the tunnel and leg coinciding. The foot is fixed against the rest in slight inward rotation. Then a separate roentgenogram is made of each joint with the tube centered exactly perpendicularly over the joint. The position of each joint on the ruler is thus accurately recorded, and measurements can be readily determined.—*George Cooper Jr., M.D.*

Sevastikoglou, John, A simple application of orthoroentgenography. *Acta orthop. Scandinav.*, 1952, *22*, 80–84.

A modification of Green, Wyatt and Anderson's "orthoroentgenography" is described. The need for special cassettes and films is eliminated.

The apparatus consists of a metallic orthogonal frame, the longitudinal bars of which are marked off in cm. and mm. Movable metallic crossbars serve as cassette holders. A plastic case fits over the frame, and both can be placed on an ordinary roentgenographic table.

The patient is placed on the pastic top with the legs parallel to the longitudinal axis of the frame. Then a roentgenogram is made of each joint with the tube centered exactly over the joint.

The measurements are obtained as follows: The part of the femur included in both the hip and the knee roentgenograms is measured with the aid of an ordinary numbered scale and the defined distance between the two cassettes is added and in this way the whole length of each femur is calculated.—*George Cooper, Jr., M.D.*

LAPIDUS, PAUL W. Congenital bilateral angulation of both bones of the leg with pes planus and plantarly flexed talus, simulating congenital talipes calcaneo-valgus; report of a case. *Bull. Hosp. Joint Dis.*, Oct., 1952, *13*, 356–368.

The author reports an unusual case of bilateral congenital medial and posterior angulation at the lower thirds of both bones of the legs, associated with pes planus and plantarly flexed talus which corrected itself spontaneously. The child was otherwise normal.

Roentgenograms were made one day after birth and at intervals until the child reached the age of seven and one-half years. At the first examination it was believed that incomplete fractures may have occurred because of the acute angulation. Subsequent films showed gradual correction of the angulation of both bones of the leg. At the last examination the original angulation was reduced to a very slight bowing, convexed medially and was slightly more marked on the left side. Irregularity of the lower ends of the diaphyses was also noted. The pre-existing plantar flexion (equinus) of the talus had by now greatly diminished. These findings were similar to those noted when the child was four years of age.

An interesting observation was a circular constriction over the posterior medial aspect of both calves above the ankles and a medial posterior dimple at the same level on the right side.—*J. N. Ané, M.D.*

KANDEL, BERNARDO. The suroplantar projection in the congenital club foot of the infant; its clinical and radiological significance. *Acta orthop. Scandinav.*, 1952, *22*, 161–173.

To obtain the suroplantar projection of the foot, the patient is postured in the vertical position with the sole of the foot horizontal and the tube placed behind the leg, angled to 40 degrees so that the ray traverses its lower quarter. Normally in the newborn infant this view shows the ossification center for the astragalus to be under the tibial metaphysis, to be round or slightly oval and to have a transverse axis. The epiphysis for the calcaneus is oval with a vertical main axis which is in perfect alignment with the longitudinal axis of the fibula. The astragalar nucleus is situated medially on the same level as the upper pole of the nucleus of the calcaneus with which it forms a right angle. The two centers are separated by a space of a few millimeters. In cases of clubfoot the tibia and fibula appear superimposed on each other due to the fact that when the rigid foot rests horizontally the whole limb rotates and bends inwardly. The calcaneus now appears under and quite near the tibial axis. The astragalus also changes its normal position and comes to lie either lateral to, or directly over the upper pole of the os calcis.

The author states that complete and lasting recovery is assured when the suroplantar view shows that the normal relationship between the tibia, fibula, astragalus and calcaneus has been established by manipulative correction. Correction of the deformity is more difficult when the epiphysis for the astragalus is hypoplastic than when it is normally formed. Treatment must be commenced immediately after birth.—*Arthur E. Childe, M.D.*

COLTART, W. D. "Aviator's astragalus." *J. Bone & Joint Surg.*, Nov., 1952, *34-B*, 545–566.

Between 1940 and 1945, approximately 25,000 fractures and dislocations were treated by surgeons working in orthopedic units of the Royal Air Force. There were 228 injuries of the talus—roughly 1 per cent of all injuries, or 6 per cent of 4,000 injuries affecting the ankle and foot. Survivors of air crashes seldom had bilateral injuries, only 10 patients having injuries to each talus. Flying accidents accounted for 106, nearly 70 per cent of the more severe lesions.

The injuries were subdivided into several groups. The fractures were classified as follows: chip and avulsion fractures; compression fractures of the head of the talus; fractures of the body; fractures of the neck. Fracture-dislocations were classified as fracture of the body with subtalar dislocation; fracture of the neck with subtalar dislocation; fracture of the neck with posterior dislocation of the body. Dislocations were of a type in which the talus was dislocated from all three joints, and there was also dislocation at the subtalar joint only. Under miscellaneous injuries was fracture-dislocation of the ankle combined with subtalar dislocation of the tarsus so that the talus was left totally dislocated. This injury is important because the talus may undergo avascular necrosis, which it will not do after either a Pott's fracture or subtalar dislocation alone. In 4 cases a fracture through the neck of the talus was associated with dislocation at the mid-tarsal joint.

In diagnosis, the importance of distinguishing between fractures and fracture-dislocations and of watching carefully for displacements of the subtalar joint is emphasized. Swelling obscures minor displacements at the subtalar joint which so frequently

occur and which it is important to recognize and reduce. Only by roentgen examination can the true state of affairs be revealed.

The important complications, as stated by the author, are infection, avascular necrosis and traumatic arthritis of the ankle or the subtalar joint. Injuries of the talus are classified according to mechanism of their production into traction injuries—direct violence injuries—and those due to extension or to flexion at the ankle joint. Dorsiflexion or plantar flexion seldom occurs alone; inversion, eversion or adduction are associated displacing forces, except in fractures of the neck of the talus, which appear to be pure dorsiflexion injuries. Dorsiflexion in one group, and plantar flexion in the other are, however, the essential and principal elements in producing the more important injuries.

The author concludes that results of excision of the talus are poor, and states that every effort should be made to preserve the body of the talus, but if its loss is inevitable a useful foot can be regained by deliberate fusion of the tibia to the calcaneum.

The paper is illustrated by numerous roentgenographic reproductions of the various types of injuries.—*R. S. Bromer, M.D.*

Bailey, Donald K. The normal cervical spine in infants and children. *Radiology*, Nov., 1952, *59*, 712–719.

In roentgenology of the cervical spine in infants and children the developmental anatomy of the cervical spine must be correlated with the roentgen appearance.

In the first cervical vertebra the neural arches fuse with the body of the vertebra at about the seventh year and before this age the line of ultimate fusion may be mistaken for a fracture.

In the axis there are four primary ossification centers (one for the odontoid, one for the body, and two for the neural arches) and prior to the fusion of these centers, between the ages of three and six years, any of the synchondroses may be mistaken for a fracture.

In the remainder of the cervical vertebrae the neural arches fuse with the body of the vertebra between the ages of three and six years. In both children and adults, the superimposition of a transverse process on one of the intervertebral spaces may cause some error in interpretation and may, in a lateral projection in very young children, simulate a compression fracture of a vertebral body.

By the age of eight years the cervical spine has with few exceptions attained an adult form.—*Harold C. Hamilton, M.D.*

Muntean, E. Zur Frühdiagnose der Lockerung im zervikalen Bewegungssegment. (On the early diagnosis of loose cervical spine segments during motion.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Nov., 1952, *77*, 553–561.

Degenerative change in the cervical spine may lead to manifold clinical symptoms. The decrease in the height of the intervertebral space is its first anatomical consequence. This decrease in height causes changes in the small joints, producing disturbance of the physiological movements between the vertebral bodies. It is possible to diagnose such abnormal motion of a cervical segment by roentgenological means.

The functional changes appear before roentgen signs of narrowing of the intervertebral space, secondary arthritis and narrowing of the intervertebral foramina are demonstrable. While there is a slight but definite alteration in the height of the normal intervertebral space during flexion and extension, the height remains unaltered when early degenerative changes have taken place. Minimal movement of the vertebral bodies on each other can also be detected in such instances. Instead of the normal lordosis, there may be a localized kyphosis at the diseased level even when no other roentgen signs are as yet present. The abnormal segment may appear fixed and immovable when roentgenograms are made in flexion and extension.—*Hans W. Hefke, M.D.*

Romanus, Ragnar, and Ydén, Sven. Diskography in ankylosing spondylitis. *Acta. radiol.*, Dec., 1952, *38*, 431–439.

It has usually been considered that a feature typical of ankylosing spondylitis is the fact that the intervertebral discs remain normal. However, in recent years it has been pointed out that the intervertebral space may diminish in ankylosing spondylitis.

One hundred and ten men with ankylosing spondylitis were studied in whom a disc space narrowing could be demonstrated. Discography was performed on 30. The method employed involved the use of a thin puncture needle inserted into the center of the disc—under fluoroscopic control. The needle passed from behind through the spinal canal. The contrast medium was injected and any rupture or prolapse of the disc could be visualized. Furthermore, if there was a protrusion of a disc, this was rendered more pronounced by the injection of the contrast substance so that any lumbago-sciatic symptoms were exaggerated.

From one to three of the lower lumbar discs, amounting to 74 in all (in the 30 individuals) were investigated. Thirty-nine were found to be normal and 35 were pathologic. Of the latter, 6 presented the appearance of an atypical rupture. In the remaining 29 discs, the "usual" pathologic disc changes of varying degree were found. In 6 patients a disc protrusion had given rise to symptoms reproducible on injection of the contrast medium.

In cases of recurrent sciatica, therefore, one must watch for incipient ankylosing spondylitis and examine the sacroiliac joints roentgenologically. Should the roentgenograms reveal sacroiliac joints indicative of ankylosing spondylitis, the possibility of a concomitant herniation of a disc cannot be excluded. —*Mary Frances Vastine, M.D.*

ROMANUS, RAGNAR, and YDÉN, SVEN. Destructive and ossifying spondylitic changes in rheumatoid ankylosing spondylitis (pelvospondylitis ossificans). *Acta orthop. Scandinav.*, 1952, *22*, 88–99.

Interest in the spinal changes of rheumatoid ankylosing spondylitis has, up to the present, been concentrated on the ossification stage and more recently on the fact that this calcification is situated in the periphery of the intervertebral disc rather than in the anterior longitudinal ligament.

The authors have reviewed the roentgenograms of 114 men with typical clinical and roentgenological findings of this condition, the majority of whom had been under observation for many years with frequent examinations. This systematic investigation has revealed varying stages of destructive lesions in practically all the cases with spinal changes. The region attacked varies in different cases and is sometimes ventral, sometimes lateral, and sometimes dorsal. Anterior spondylitis usually appears in the upper and lower parts of the anterior surface of the vertical body. First a slight roughening of the contour can be seen and a decreased calcium density which progresses to a true destruction. The more compact rim of the body is then sometimes left like a spike undermined by the lytic defect, which in the lateral view involves one-third of the anterior edge of the body. The same changes are often seen on two vertebrae on either side of a disc. Later on, the spike of the rim also disappears and the edge of the body appears to be worn away, thus changing its anterior contour from concave to straight—"square vertebra." At the same time, an increased calcium content often appears in the vertebral margin. In the intermediary stage one sometimes finds both destruction with erosions and calcification with bony proliferations. Secondary calcification and ossification in the healing phase are often so marked that the vertebral body is rebuilt in the destroyed area, and the newly formed bone finally becomes one with that of the original bone.

Anterior spondylitis also attacks the intervertebral discs, and in many cases they beocme narrowed. Sometimes this can be explained by disc ruptures but in other cases discography reveals that marked degeneration has occurred with the production of irregular cavities in the disc. Histological examination of excised material has shown inflammatory changes in the peripheral part of the disc.

These two stages, primary destruction and erosion and secondary calcification, ossification and bone proliferation are also to be found in the sacroiliac joints, pubic rami, ischial tuberosities, iliac crests, sternal synchondrosis and the sternoclavicular and acromioclavicular joints.—*Arthur E. Childe, M.D.*

JAFFE, HENRY L. Skeletal manifestations of leukemia and malignant lymphoma. *Bull. Hosp. Joint Dis.*, Oct., 1952, *13*, 217–238.

Leukemia may be of the myeloid, lymphatic or monocytic type and may run an acute, subacute or chronic course.

Acute leukemia simulates acute infection and is more common in childhood. In some cases the symptoms of acute leukemia may be primarily of skeletal origin. On the other hand, in the case of chronic leukemia, skeletal involvement occurs infrequently and late in the course of the disease. The leukemic child often complains of pain and tenderness in the long bones and migratory pains and, at times, swelling of joint regions. Roentgenographic findings may prove of value in the differential diagnosis, especially in the aleukemic phase.

From 50 to 60 per cent of leukemic children will show bone changes on the roentgenograms. The earliest finding consists of a narrow transverse zone of increased radiolucency at the shaft ends of long bones where endochondral bone growth is most active. These areas are also noted in scurvy and other severe illnesses.

Periosteal new bone deposition, osteoporosis, variable areas of osteolysis, infractions and vertebral compressional collapse are also noted on the roentgenograms. While the bone changes may simulate metastases from neuroblastoma, the roentgenographic evidence of skeletal involvement in neuroblastoma is not likely to include involvement of bones below the knees and elbows. In leukemia these areas may be affected.

In some cases of leukemia the bone changes may consist of increased radiopacity of bones without evidence of periosteal proliferation. It is believed that these children represent cases of osteopetrosis (marble bones) in whom leukemia has developed as a terminal phase.

It is interesting that during remissions and therapy the bone lesions regress and the radiolucent zones are replaced by radiopaque bands similar to those noted in poisoning by heavy metals. With the onset of the terminal phase the original skeletal lesions reappear.

In adults, bone lesions are evident in from 8 to 10 per cent. Rarefaction, osteolytic foci, periosteal new bone deposition and fractures, especially of ribs, may occur. Osteosclerosis of a generalized type is rare.

The various primary cancerous conditions arising in lymph nodes are grouped together as the malignant lymphomas. These include Hodgkin's disease,

lymphosarcoma, reticulum cell sarcoma and giant follicle lymphoma. Males are more frequently affected and the cervical lymph nodes are the most common location.

In the malignant lymphomas, the bones are involved by direct extension from affected lymph nodes or by metastatic spread by way of the vascular and/or lymphatic channels. There is no characteristic roentgenographic picture for areas of bone involvement in Hodgkin's disease. Osteolytic destruction of one or more vertebral bodies may cause their collapse. Radiopaque areas may be intermingled with the radiolucent osteolytic foci and periosteal new bone formation may be present. The osteoblastic reaction may be so pronounced that one notes the picture of a so-called "ivory vertebra."

In lymphosarcoma, clinically manifest bone lesions are observed in about 10 per cent of the cases. In contrast to Hodgkin's disease, it is only exceptionally that attention is first directed to the presence of lymphosarcoma by complaints of skeletal involvement. As in Hodgkin's disease the vertebral column is most frequently involved. It is possible in Hodgkin's disease and in lymphosarcoma that the patient may complain of skeletal pain before local bone destruction can be shown roentgenographically.

The giant follicle lymphoma, as such, does not appear to be associated with skeletal involvement. When it becomes malignant the character of the disease becomes that of lymphosarcoma.

In reticulum cell sarcoma localized osteolytic lesions may be evident in from 10 to 15 per cent of cases. The areas and pattern of involvement simulate the findings in lymphosarcoma.

Irradiation with from 600 to 1,500 r will usually relieve the pain at the site of a clinically manifest bone lesion. Such therapy may have to be repeated if the patient survives as the lesion usually becomes reactivated.

While there is considerable speculation as to whether some of the malignant lymphomas may originate in bone it is believed that a skeletal area may be the point of departure in reticulum cell sarcoma. The long bones, such as the femur, tibia and humerus, in individuals under forty years of age are most frequently involved. The roentgenographic picture is not distinctive. While the lesion is essentially osteolytic, patchy osteolytic areas may be intermingled with some areas of patchy radiopacity. Although there is no bone formation in the tumor, periosteal bone may be stimulated when the tumor breaks through the cortex.

Clinical and roentgenographic studies are not sufficient to make a diagnosis of primary reticulum cell sarcoma since the diagnosis depends upon histologic examination of the lesion. The differential diagnosis between reticulum cell sarcoma and Ewing's sarcoma is difficult—*J. N. Ané, M.D.*

Roaf, Robert. Ewing's tumour affecting the medial cuneiform bone; report of a case. *J. Bone & Joint Surg.*, Nov., 1952, *34-B*, 640–641.

The author states that the characteristic appearances of Ewing's tumor in a long bone are well known, but it is not so generally realized that the changes occur when a short bone is affected and are by no means typical. For this reason, he reports a case of a tumor of the medial cuneiform bone in a boy fourteen years of age who complained of pain in his left foot. There was no obvious deformity of the foot and all movements were full, but there was slight edema and increased warmth of the foot on its medial aspect. The roentgenogram showed a dense sclerotic process. A small hole was made in the cortex of the bone after being exposed and gray semi-solid material was scooped out. This was diagnosed as Ewing's tumor on histological examination. Amputation below the knee was performed. The patient remained well for two years, but at that time evidence of pulmonary metastases was found. He died just over three years after amputation.

Professor Willis in his report of the histological sections said that he agreed that the section showed changes which are commonly described as Ewing's tumor. He regards Ewing's tumor as not a single pathological entity, but rather a clinical syndrome which can be produced by several different kinds of tumors. One of the most frequent of these in young subjects is metastatic neuroblastoma, from primary growths in the adrenals or sympathetic ganglia. In his opinion the cytology of the tumor in this case strongly suggested neuroblastoma, although he did not consider rosette formation distinct enough to justify a dogmatic diagnosis. Since no autopsy was obtained its nature remained uncertain.

Professor Baker reported that he regarded bone tumors of the type shown in the sections as tumors of the "Ewing type" by which he meant an undifferentiated tumor composed of cells with little cytoplasm and with fairly uniform and oval or rounded nuclei, not bone-producing but apparently arising in bone. The tumor was certainly malignant and there seemed to be a reasonable probability that it was a primary bone tumor belonging to the Ewing group.—*R. S. Bromer, M.D.*

Valls, José, Muscolo, Domingo, and Schajowicz, Fritz. Reticulum-cell sarcoma of bone. *J. Bone & Joint Surg.*, Nov., 1952, *34-B*, 588–598.

In this paper the authors report the results of their study of 10 cases of primary reticulum cell sarcoma of bone and compare the clinical, pathological and roentgenographic features with those of 35 cases of Ewing's sarcoma. In their microscopic studies, Hortega's staining techniques were used in addition to the usual orthodox methods. Histologic studies were rendered easier by invariable absence of necrotic

areas seen in Ewing's sarcoma. Hortega's specific technique showed in the cases of reticulum cell sarcoma a wealth of the reticuloendothelial elements and their even distribution among the more differentiated cells. Their shape was variable, predominantly ramified, although sometimes they were ameboid or rounded, and their association with the walls of the blood vessels was evident. The distribution of the reticulin fibrillar network, the authors considered was a fundamental feature of the tumor. Starting at the adventitia of the blood vessels as a close mesh, it gradually became more open, though always maintaining the reticulum tendency of forming small or medium-sized areolae containing isolated or small groups of tumor cells. In contrast, Ewing's sarcoma by ordinary staining reveals a compact mass of cells of uniform shape, with rounded or oval nuclei, indistinct nucleoli, and usually ill-defined and scanty cytoplasm. In such tumors Hortega's techniques show the reticulin fibers circumscribing large areas containing many cells, forming lobules into which no fibrillae (or very few) penetrate. Moreover, the morphologically different reticulohistiocytic elements are very rare among the tumor elements and somewhat more numerous among the reticular and collagen fibrillae surrounding the lobules.

The authors noted that the reticulum cell sarcomas did not affect the general condition of the patient. The onset was insidious and the evolution was slow. Pain was the initial symptom although it never attained the intensity found in some other malignant growths.

On roentgen examination, the tumor was essentially osteolytic. In the long bones, the reticulum cell sarcoma arises in the marrow of the epiphysis or metaphysis. It then spreads rapidly toward the cortex, which it destroys, and then invades the soft tissues. There is a total absence of the spicular images apparent in Ewing's sarcoma and some of the osteogenic sarcomas. The authors consider the absence of reaction on the part of the cortex and the periosteum as a valuable aid in differential diagnosis. The roentgenographic evidence of total lysis was not always found. Sometimes bony trabeculae remained within the areas of destruction and produced a multilocular appearance such as is seen in the giant cell tumors and in hydatid disease. The progress of the tumor as was shown in the roentgenograms was rapid and the osteolytic process ended by affecting a karge area of the bone in which it began.

The authors think that the primary reticulum cell sarcoma of bone is very radiosensitive, but radiation therapy does not constitute a guarantee against recurrence which unfortunately is relatively frequent. In one of their cases a lung metastasis appeared as long as ten years after the onset of the disease. This observation led them to think that, despite the relatively benign character of the tumors and their marked radiosensitivity, a wide excision of the growth is advisable.—*R. S. Bromer, M.D.*

McCORMACK, LAWRENCE J., IVINS, JOHN C., DAHLIN, DAVID C., and JOHNSON, EINER W., JR. Primary reticulum-cell sarcoma of bone. *Cancer*, Nov., 1952, *5*, 1182–1192.

The authors report from the Mayo Clinic a series of 32 cases of primary reticulum-cell sarcoma of the bone which may closely resemble Ewing's sarcoma. They believe that there are clinical and microscopic criteria which justify the consideration of this tumor as a separate entity.

The presenting symptoms are pain and swelling; in 76 per cent of the cases these symptoms had persisted for less than a year. The lesions are usually located in the extremities and in most cases are solitary. Roentgenographically, there is evidence of osteolytic destruction of the bone.

Diagnosis is made by biopsy, and results seem to indicate that the therapy should consist of surgery and irradiation.

Grossly, the tumor is large and soft involving the bone either concentrically or eccentrically. There is bone destruction but no evidence of joint invasion.

Microscopically, the typical reticulum cell is present in varying amounts. It varies in size from two to four times the size of a lymphocyte and has a faintly eosinophilic cytoplasm. The nucleus is lobular and occupies most of the cell. The cells are embedded in a fibroblastic stroma.

The authors believe that the prognosis of a well treated primary solitary reticulum-cell sarcoma is much better than in multiple lesions of this type and more favorable than in other primary bony neoplasms. Therefore, its segregation is of value.—*George L. Sackett, Jr., M.D.*

WAUGH, W. Fibrosarcoma occurring in a chronic bone sinus. *J. Bone & Joint Surg.*, Nov., 1952, *34-B*, 642–645.

The occurrence of carcinoma is a well recognized complication of a chronic bone sinus, but the occurrence of a fibrosarcoma is unusual. In the case reported in this paper, the clinical diagnosis was that of a carcinoma and the biopsy report of fibrosarcoma was unexpected. The tumor was as shown by the histological findings, arose from connective tissue and not from the epidermis. Roentgenograms of the lesion in the lower end of the femur showed a large cavity surrounded by sclerosed bone. Periosteal new bone formation extended half way up the shaft of the femur. There was evidence of bony ankylosis at the knee joint.

The patient was a man, sixty years of age. In 1903, he had injured his knee playing football and the knee had been operated upon. Osteomyelitis developed and he was left with a chornic sinus on the outer surface of the left thigh, and his knee became stiff. The sinus continued to discharge after a further operation in 1936. On examination, when admitted to

the hospital, a fungating mass was present which was 4 inches in diameter with a base 2 inches wide at the site of the sinus. The growth was heavily infected and bled easily but it felt firm. The inguinal lymph nodes were not palpable.

The author states that no conclusion can be drawn from the few cases published as to the relative prognosis between epithelioma and sarcoma. The etiological factors and the natural history of the condition are probably very similar in each. His patient died with symptoms suggesting a severe gastrointestinal hemorrhage, two months after amputation. No postmortem examination could be obtained.—*R. S. Bromer, M.D.*

## Blood and Lymph System

Parker, Joe M., Russo, P. E., and Oesterreicher, D. L. Investigation of cause of lymphedema of the upper extremity after radical mastectomy. *Radiology*, Oct., 1952, *59*, 538–545.

The authors have been routinely binding the arm following radical mastectomy to prevent the development of lymphedema. In an effort to show why such a procedure prevents lymphedema, preliminary work with venous pressures and venograms has been done. The small series cited shows a temporary (1 to 4 months) postoperative "hour-glass" constriction of the axillary vein in the region of the junction of the subscapular vein which is ligated at the time of surgery. The constancy of this defect suggests the formation of a mural thrombus but no postmortem evidence has been available to date. It is suggested that this thrombus formation may be the initiating factor in the development of lymphedema.—*Martin B. Goodwin, M.D.*

Hunt, Alan, H. Portal venography. *Proc. Roy. Soc. Med.*, Oct., 1952, *45*, 722–723.

Complete investigation of a case of portal hypertension is possible only when the abdomen has been opened and the liver and spleen and its attachments, the collateral anastomotic channels and the portal venous pressure have been investigated. This procedure usually enables one to determine the site of obstruction; however, venography is necessary to show the extent of the obstruction, the state of the portal venous tree and what varicose transformation has occurred if the obstruction is extrahepatic. Venography shows whether or not portal thrombosis is present in addition to cirrhosis and where the bulk of the portal blood is flowing. If previous portal system anastomosis has been performed, the effectiveness of this shunting procedure can be determined by venography. Venography is considered essential in about 20 per cent of the cases. It is never possible to be certain that venography will not be of assistance in any case. Venography shows the functional state of the splenic and portal vessels and may eliminate the difficult dissections required for physical inspection of the portal and splenic veins.

A suitable technique for portal venography is rapid injection of 30 cc. of 70 per cent diodone, using a 50 cc. syringe with as large a needle as can be safely inserted in the vein. The roentgenogram is made at the end of the injection. The film is placed in a casette tunnel under the patient, the film edges reaching from the nipple line to the umbilicus. It takes only two to three minutes to perform the entire procedure. A trial roentgenogram for exposure factors is advised before the operation. Examination of children should be done with a reduced amount of the contrast medium, proportionate to their size. No untoward side-effects have been observed.—*Donald R. Bernhardt, M.D.*

Surington, Cyril, T., and Jonas, August F., Jr. Intra-abdominal venography following inferior vena cava ligation. *A.M.A. Arch. Surg.*, Oct., 1952, *65*, 605–610.

There have been conflicting reports regarding the value of ligation of the inferior vena cava for the prevention of recurrent emboli due to venous thrombosis in the lower extremities or pelvis. Development of massive edema, varicosities, and leg ulcers has been reported following the ligation.

The authors, in an effort to demonstrate the collaterals and their relative importance following ligation of the inferior vena cava, have developed a technique of venography. A polyethylene tube is inserted into the greater saphenous vein and 50 cc. of neo-iopax or diodrast is quickly injected into the vein. Near the completion of the injection roentgenograms are made. The method was used on 3 patients two to three years following ligation of the inferior vena cava and on a number of patients undergoing lumbar sympathectomy. The inferior vena cava was temporarily occluded in this group by pinching it with the thumb and finger.

The principal collateral routes are as follows: (1) ascending lumbar veins communicating with the azygos and hemi-azygos veins in thorax, (2) ventebral veins, (3) ovarian veins, (4) ureteral veins, and (5) superficial trunk veins, which are the least important.

From these studies, it is inferred that little disability will result following ligation unless there has been pre-existing vascular disease in the collaterals—*Wallace M. Roy, M.D.*

Sotgiu, G. Cacciari, C., and Frassineti, A. Splénoportographie. (Splenoportography.) *Presse méd.*, Oct. 1, 1952, *60*, 1295–1296.

Following the usual splenic puncture, 20 cc. of the radiopaque material is injected into the spleen. The authors use a 70 per cent preparation of diodone

(Pielosil Glaxo). The injection is made in about two to four seconds because the opacity dissipates rapidly disappearing from the splenic and portal veins in three seconds, from the liver in four to six seconds and from the spleen in ten to twelve seconds unless there is stasis. No special apparatus is used for injection. The injection is made with care to avoid disruption of splenic tissue but it must be made steadily.

Roentgenograms are made between the end of the injection and up to four seconds. Exposures of one second are used. The injection is well tolerated and none of the patients have registered complaints. There are no risks beyond that of an ordinary splenic puncture. Adrenalin is not used to contract the spleen.

The results in cases of chronic myeloid leukemia, thallassemia, splenic thrombophlebitis and splenic cirrhosis are illustrated.—*Marcy L. Sussman, M.D.*

PEREIRA CALDAS, JOSÉ. A arteriografia dos membros, da aorta abdominal e dos seus ramos. (Arteriography of the extremities, of the abdominal aorta and its branches.) *Acta ibér. radiol. cancerol.*, July–Sept., 1952, *1*, 279–358.

This report was read as part of a symposium on angiography at the Second Congress of Electro-Radiologists of Latin Culture and the Second Hispanic-Portuguese Congress held in 1952.

In the introduction the author reviews the remarkable contributions which have been made by the Portuguese school to this important branch of roentgenology. Thus in 1927, Egas Moniz, professor of neurology at the University of Lisbon, originated cerebral arteriography, followed soon by Reynaldo dos Santos, professor of surgery and urology of the same University, who in 1928 performed the first puncture of the abdominal aorta and in 1929 with other collaborators (of which the author was one) published his now famous work on visualization of the abdominal aorta and arteriography of the extremities. The puncture of the aorta permitted the roentgen demonstration of all the infradiaphragmatic organs, with the exception of the pancreas. In 1932, Lopo de Carvalho, professor of phthisiology of the University of Lisbon, developed angiopneumography and shortly thereafter angiocardiography by injecting opaque media into the lesser circulation through the right cavities of the heart. Phlebography, a natural sequence of arteriography, was established as a major method of examination by J. Cid dos Santos and, more recently, Aleu Saldanha devised a method of opacification for the study of the intermediary circulation between the arterial and venous capillaries, or the so-called tissue plasma circulation.

The author himself, as professor of radiology of the University of Lisbon, was from the beginning intimately associated with most of these investigations, working out various techniques, designing and constructing different types of apparatus for rapid exposure (some of which now bear his name, as, for example, the Pereira Caldas radiocarrousel) and testing an imposing array of opaque media for the most efficient visualization. The problems encountered gradually assumed such vast proportions that a division of the many methods used into more specialized angiographic branches became inevitable.

Based on such considerations, the author in the present report deals only with abdominal aortography and arteriography of the extremities, a domain in which he has the greatest experience. The subject is divided into four chapters: (1) history; (2) technique; (3) accidents; and (4) interpretation and results.

(1) *History*. Attempts to opacify the arteries of animals and human cadavers had already been begun in 1896 and continued assiduously by a number of investigators for the next twenty-five years. In 1923 and 1924, Sicard and Forestier obtained arteriograms by injecting lipiodol and were soon followed by Berberich and Hirsch, who used strontium bromide, and by Brooks, who for the first time injected sodium iodide into an artery. The procedure, however, failed to emerge from the experimental stage until 1927 to 1929 when Egas Moniz and Reynaldo dos Santos made their above mentioned fundamental contributions. Even after that, for two years the Portuguese school remained alone in advocating peripheral arteriography and, more particularly, abdominal aortography for clinical use. Some progress was made after the publication of the monographs by Reynaldo dos Santos, Lamas and Pereira Caldas in 1931 and by Reboul in 1935 but it was not until 1945 that the procedure was embraced more generally. Since then numerous outstanding articles appeared in the world literature attesting to the clinical value of peripheral arteriography and abdominal aortography.

(2) *Technique*. The injection technique used by the Portuguese school is described in detail and compared with other similar techniques. The injection under manual pressure is condemned. Instead the author uses the constant pressure apparatus devised by R. dos Santos which permits preliminary adjustment of the pressure to the desired level. The size of the needle used for puncture, as well as the amount of the injected opaque solution, varies according to the caliber of the vessel injected.

In 1942, the following schematic procedure was devised: (A) Arteriography, (a) femoral artery—puncture in the groin; pressure of 1 to 1.5 kg.; needle of 0.9 to 1 mm. external diameter; 20 cc. opaque solution; visualization of the arteries of the thigh and knee in 7 seconds, of the leg in 8 seconds and of the foot in 9 to 11 seconds; (b) subclavian artery—pressure of 1 kg.; needle of 0.9 mm. external diameter; 15 cc. opaque solution; visualization of the arteries of the shoulder in 3 seconds and of the arm in 5 seconds; (c) brachial artery—puncture in the middle of

the arm; pressure of 0.5 kg.; needle of 0.8 mm. external diameter; 10 cc. opaque solution; visualization of the arteries of the hand in 8 seconds; (B) Abdominal aortography, pressure of 1.5 to 2 kg. ; needle of 1.2 mm. external diameter and 12 to 14 cm. length; 20 to 25 cc. opaque solution. For the injection of the aorta formerly two sites were chosen, one at the level of L2 and the other at the level of D12. At the present the puncture of the vessel is made at the level of D10 or D11, so as to avoid accidental injection of the celiac artery or of the right renal artery. The patient is placed in ventral decubitus and the needle is introduced under the left twelfth rib, four fingers lateral from the midline. It is directed first perpendicular to the skin until the mass of muscles is passed, then upward and inward toward the body of D10 or D11. At a depth of 12 cm. the mandrin is withdrawn and the needle is advanced a little farther, usually entering the aorta with ease.

The author has tested practically all of the opaque media available on the market and has arrived at the conclusion that the ideal medium has not been found as yet. Until then he prefers the organic iodide solutions and as a rule employs 80 per cent perabrodil M for arteriography of the extremities, and skiodan diluted to 100 per cent in physiologic serum for aortography.

The roentgenographic technique and the various tables provided with rapid cassette changers are also described at length.

(3) *Accidents.* These may consist of (a) complications resulting from the puncture of the vessel; (b) sequelae of the technique of injection; and (c) effects of the injected opaque solution. They are discussed thoroughly and the ways to prevent them are indicated.

(4) *Interpretation and results.* In this extensive chapter the author evaluates the various roentgen findings and gives an up to date account of the results which might be expected from this type of examination not only in lesions of the vascular system proper but also in many other pathologic processes reflecting aberrations or disturbances of the blood supply.

The article is profusely illustrated with reproductions of beautiful arteriograms of the extremities and aortograms portraying the characteristic roentgen findings in a great variety of conditions.—*T. Leucutia, M.D.*

Salleras, Víctor. Flebografía de las extremidades inferiores. (Phlebography of the lower extremities.) *Acta ibér. radiol. cancerol.*, Oct.–Dec., 1952, *1*, 475–496.

The author gives an extensive review of the historical development, of the various technical procedures and of the presently accepted indications of phlebography of the lower extremities.

Chronologically he distinguishes two periods, the first extending from 1902 to the time of the publication in 1938 of the fundamental work of Cid dos Santos who definitely established phlebography as a major method of exploration of the vascular system, and the second from 1938 to the present. The salient contributions made by the various investigators during these two periods are cited and commented upon.

Of the contrast media used for opacification are listed: sodium iodide (30 per cent), thorotrast, uroselectan, diodrast, ioduron, tenebryl and umbradil. The author uses exclusively a 35 per cent aqueous solution of umbradil which is the diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid. This medium gives excellent contrast, is devoid of side reactions, does not produce thrombosis and is harmless in case of extravasation. It is the best medium available in Spain.

The technical procedures considered include: (1) direct phlebography and its many modifications, among which are phlebography of the superficial venous system, phlebography of the deep venous system according to the techniques of Cid dos Santos, Olivier, Massell and Ettinger (used by the author) and others, phlebography of the iliac veins, vena cava and pelvic veins, retrograde phlebography and dynamic or functional phlebography; (2) percutaneous retrograde functional phlebography which the author performs with two different techniques. He injects the internal saphenous vein for the visualization of the deep venous system of the thigh and the external saphenous vein for the visualization of the deep venous system of the leg and obtains passage of the opaque medium into the deep veins by increasing the pressure during the injection by means of a strictly physiologic mechanism which consists of making the patient cough twice in the former procedure and by making him exert a certain muscular force (according to Ferreira) in the latter; (3) indirect phlebography which is usually carried out with the standard arteriographic technique; and (4) intraosseous phlebography which is ordinarily preferred when there is danger that the wound following open injection may not heal and when a percutaneous injection is impossible. The bone puncture is made in the lower end of the tibia, internal malleolus, external malleolus or the os calcis for visualization of the deep veins of the lower extremity and in the pubic bone, ischium, greater trochanter or the upper anterior iliac spine for visualization of the pelvic veins. Although all advocates of the transosseous injection claim that the method is innocuous, the author found that it is invariably associated with severe pain unless general anesthesia is used.

The indications and use of phlebography are discussed at length in the following conditions: congenital lesions of the veins, such as arteriovenous fistulas and angiomas; traumatic lesions of the veins; varices; insufficiency of the deep venous system; and thrombophlebitis.

A rich bibliography is appended.—*T. Leucutia, M.D.*

SALDANHA, ALEU. Estudo radiologico de circulação plasmo tecidular. (Roentgen study of the tissue plasma circulation.) *Acta ibér. radiol. cancerol.*, Oct.–Dec., 1952, *1*, 391–424.

The author coins the name of tissue plasma circulation for the intermediary circulation which exists between the arterial capillaries, on the one side, and the venous and lymphatic capillaries, on the other. It is now generally accepted that the composition of the tissue plasma differs from that of the blood plasma and of the lymph.

Since 1942 he, realizing the physiologic and pathologic importance of the connective tissue, studied by means of various roentgenographic contrast methods the anatomic distribution of the various spaces formed by this tissue, its function and especially the circulation of the interstitial fluids. In former publications he reported on the results obtained by opacification in dogs and human cadavers of some of the internal intrafascial spaces, as for example, the perivascular sheaths (thecagraphy), the areolar connective tissue layer surrounding the gallbladder, the perirenal fascia, etc.

In the present excellent article, the author pays attention to the external intrafascial spaces, since they permit an easier study of the tissue plasma circulation which is his main objective. The superficial fascia is commonly described as a thin and open lamina running parallel to the skin and lying between the panniculus adiposus and the subcutaneous cellular tissue. When this latter is abundant several supplementary laminae may be present linked together by connective tissue septa which give rise to the so-called external intrafascial spaces. According to Pés-Larrive these spaces resemble the areolar interstices of the subperitoneal fascia which covers the kidneys, bladder, rectum and blood vessels and is thus part of the internal fascia.

The method consists of the injection immediately beneath the skin of 10 cc. of an isotonic iodized solution usually employed in urography (tenebril perabrodil, diiodone, etc.). Serial roentgenograms in tangential projection are made 10, 30, 60 and 90 minutes after the injection and the various factors governing the absorption of the contrast medium are studied.

The author distinguishes three phases on the roentgenograms: (1) phase of reticulation, corresponding to the collection of the injected contrast medium in the network of intrafascial spaces. This starts immediately after the injection and is normally completed within 15 to 30 minutes; (2) phase of extension along the intrafascial spaces. This occurs simultaneously with the former but lasts somewhat longer, depending on the quantity and viscosity of the injected material and on the pressure within the tissues; and (3) phase of true absorption with gradual clearing of the opacification, due to passage of the opaque medium into the venous capillaries and under certain circumstances into the lymphatic capillaries. The duration of all three phases corresponds to approximately 60 to 75 minutes.

Comparative analysis of a large number of roentgenograms permitted the author to draw the following conclusions:

The morphologic aspect of the image varies with the individual, sex, nutritional state and age.

The physiologic aspects depend primarily on the modifications of the blood circulation and on various tissue factors.

Increase of the venous pressure widens the intrafascial spaces, delays slightly the reticulation and above all prolongs the time of absorption.

Vasoconstriction narrows the intrafascial spaces, limits the extension of the opaque medium and retards the absorption.

Vasodilatation enlarges the intrafascial spaces, delays the reticulation, diminishes the contrast by dilution and impedes the absorption although later it accelerates it.

Muscular contraction, by accelerating the blood circulation, speeds up the absorption.

The passage of the opaque medium from the tissue through the intrafascial spaces into the blood is a roentgenologic measure of the blood-parenchyma barrier.

Hyaluronidase, or the Duran-Reynals spreading factor, by increasing the permeability of the connective tissue, enhances the accumulation, accelerates the absorption and increases the diffusion of the opaque medium in the intrafascial spaces.

Certain pathologic conditions may also affect the tissue plasma circulation, thereby leading to various roentgen appearances. Among these are: hypothyroidism with simple obesity, myxedema or compensated myxedema, Cushing's syndrome, arterial obliterations, varices, and the edemas. In this latter group two types of images are obtained: (1) the reticular type, with large intrafascial spaces and marked delay of absorption due apparently to the difficulty of the tissue-plasma fluid to return to the general circulation; and (2) the spheroid type, consisting of homogeneous opacity with diffuse borders and late or absent reticulation due to a structural obstacle to the tissue-plasma circulation. The injection of hyaluronidase in edematous tissue likewise leads to two types of reaction: (1) if no mechanical factor of a vascular nature is present, it produces reticulation, narrows the intrafascial spaces and greatly accelerates the absorption whereas (2) if such a factor exists, it enlarges the intrafascial spaces and paradoxically it prolongs the time of absorption.

The article is illustrated with reproductions of thecagrams and numerous beautiful serial roentgeno-

grams depicting the various points discussed.—*T. Leucutia, M.D.*

Barnett, William E., Moorman, Warren W., and Merrick, Ben A. Thrombotic obliteration of the abdominal aorta: a report of six cases. *Ann. Int. Med.*, Nov., 1952, *37*, 944–965.

The authors review the literature and clinical features of thrombotic obliteration of the abdominal aorta. Seventy-six such cases have been reported and the authors add an additional 6 cases.

In many instances the thrombotic obliteration of the aorta resembles coarctation of the aorta or obliterative vascular disease of the lower extremities. The late stage of the disease at time of diagnosis usually restricts treatment to that of palliative therapy.—*Allison E. Imler, M.D.*

Doss, A. Keller. Recent improvements in translumbar aortography. *J. Urol.*, Dec., 1952, *68*, 950–952.

This article calls attention to the need of an ideal radiopaque medium for aortography and to other technical improvements. At the present time, the author feels that 70 per cent urokon sodium is the drug of choice. It is the least toxic of all of the media and its density compares with that of 80 per cent sodium iodide. Urokon does produce some arterial spasm but this is a minimal side-effect. Recently, a thin-walled needle has been developed for use in aortography. This needle has an inside gauge bore of 17 with an outside diameter no larger than 18 gauge.

The author points out the importance of technically good aortograms and also the limitations inherent in the interpretation of technically inadequate films.—*George W. Chamberlin, M.D.*

Tiwisina, Th. Die Vertebralis-Angiographie und ihre diagnostische Bedeutung. (Vertebral angiography and its diagnostic significance.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Dec., 1952, *77*, 662–671.

Vertebral angiography is particularly suitable for the demonstration of supra- and subtentorial lesions, especially those in the occipital lobe, main stem, or cerebellum. Since the posterior cerebral artery is a branch of the carotid syphon in only 10–20 per cent of the cases, the author prefers this approach to carotid angiography. Furthermore, cerebellar tumors are diagnosed by carotid filling only in the presence of marked internal hydrocephalus. This method is also preferable to ventriculography because vertebral angiography causes no increase in the intracranial pressure.

The vertebral artery is entered either by exposure or percutaneous puncture. To avoid a rupture of the vessels, only 10 cm. is injected before each exposure. Roentgenograms are made in these planes: posteroanterior, lateral, and basal.

The complications include hemorrhage into the tumor, hypoxemia, and thrombosis (the latter did not occur in the author's series of 636 angiograms).

The following conditions were diagnosed by this method: congenital and traumatic aneurysms; hemangioblastoma; vascular lesions, such as endarteritis obliterans, sclerosis, and lues; anomalies; gliomas; tumors of the third ventricle; supra- and subtentorial meningiomas.

Excellent diagrams and reproductions of angiograms clearly indicate normal and abnormal anatomical details.—*Joseph Zausner, M.D.*

Scarinci, C., Gianturco, E., and Notario, P. L'intérêt de l'angiopneumographie pour l'exploration de la circulation artérielle pulmonaire chez l'homme dans l'anoxie temporaire. (The value of angiopneumography in the exploration of the pulmonary arterial circulation in man during temporary anoxia.) *Presse méd.*, Nov. 15, 1952, *60*, 1550–1551.

Several authors have produced evidence to suggest that occlusion of a pulmonary artery, even in bronchial carcinoma, might be functional. There has also been the theory that pulmonary arteritis is a necessary intermediary in right ventricular insufficiency of pulmonary origin. It is well known that pulmonary hypertension is found regularly in this condition.

Stuhl and his colleagues conclude that the disturbance in pulmonary arterial circulation which is present with constriction of the distal bronchus is a function of the severity and duration of the respiratory insufficiency. The vasoconstriction may be functional.

The authors performed angiopneumography in a normal subject in whom a temporary anoxia was produced by bronchial occlusion with a balloon. They demonstrated that a full correlation exists between ventilation and pulmonary arterial circulation. They confirmed the suggestion of Stuhl and others that a disturbance in the pulmonary arterial circulation is of the same nature as the general circulatory response to all causes of altered ventilation. —*Marcy L. Sussman, M.D.*

Wickbom, Ingmar. Thoracic aortography after direct puncture of the aorta from the jugulum. *Acta radiol.*, Nov., 1952, *38*, 343–349.

The method of aortography which the author describes is performed with the patient in the supine position, preferably under general anesthesia. The highest level of the aorta is indicated on the skin. A needle 12 cm. in length is used for the puncture which

is made above the right clavicle just lateral to the common carotid artery. The distance from this point to the highest point of the aorta is marked on the needle with a small metal ring which is movable along the needle. The needle is directed almost parallel to the course of the common carotid and the innominate arteries, *i.e.*, downwards and slightly to the left and backwards, passing immediately behind the first rib. When pulsations are felt at the needle point, the wall is punctured and the needle is introduced about 1.5 cm. farther. The author injects 30 to 40 cc. of Diodone 70 per cent, the injection time being about three seconds. He uses a cassette changer which allows for the exposure of ten pairs of films (at right angles to each other) in ten seconds.

So far the method has been used in 8 cases. In concluding, the author states that "the method has certain advantages as compared to other techniques: it is simple and not time-consuming and no vessel is ligated. The risk of hematoma development and extravascular deposition of the contrast medium is minimized if the technique is properly executed."—*Mary Frances Vastine, M.D.*

WICKBOM, INGMAR. Death following contrast injection into the thoracic aorta; case report. *Acta radiol.*, Nov., 1952, *38*, 350–354.

The contrast media used nowadays for angiocardiographic examinations are almost all composed of 3,5 diiodo-4 pyridine-N-acetic-dietanolamin. The preparation is marketed under names such as umbradil, pyelosil, diodrast, diodone and perabrodil. It has many advantages but is not ideal mainly because of its irritating effect on the arterial wall. The substance causes vasoconstriction followed by dilatation. It has been shown by animal experiments that the wall of the cerebral vessels may be temporarily damaged by the contrast medium causing a breakdown of the blood-brain barrier. This damage is clinically illustrated by severe reactions, even deaths, following cerebral angiographies. There are also cases reported in which injection of highly concentrated contrast medium into the mesenteric artery and other branches of the abdominal artery of similar size proved fatal. Judging from the literature, however, it seems that the heart and the aorta tolerate even highly concentrated contrast substances of the type fairly well.

The author reports a case in which death followed thoracic aortography after percutaneous puncture of the aorta from the jugulum. There was a serious reaction to the contrast injection but none to the puncture; at autopsy no damage, attributable to the latter, could be found. The fatal outcome was probably due to the contrast medium which remained in the coronary arteries for at least seven seconds.—*Mary Frances Vastine, M.D.*

WALSH, FRANK B., and SMITH, GEORGE W. I. The ocular complications of carotid angiography. 2. The ocular signs of thrombosis of the internal carotid artery. *J. Neurosurg.*, Sept., 1952, *9*, 517–537.

Angiography of the ophthalmic artery has not proved to be of much diagnostic value because in only about one-half of the normal carotid angiograms is the ophthalmic artery visualized and, even when it can be seen, its course is so variable normally that recognition of abnormalities is very difficult.

The flushing and pain in the face which accompany carotid angiography is the result of the presence of the contrast medium in the external carotid artery, while the pain in and about the eye is an indication that the medium has entered the internal carotid artery. The flash of light sometimes described by patients who have undergone the procedure of angiography is due to retinal irritation. It is a rare symptom. The cause of the pupillary changes is unknown. No feasible explanation has ever been offered. Transient narrowing of the retinal vessels with subsequent widening is reported by Schurr. Why there is no blurring of vision (and apparently there is none) accompanying these vascular changes is not explained. Petechial hemorrhages in the skin of the face, the conjunctiva and the retina have been observed in a high percentage of cases. One of these areas showed hemorrhage in 86 per cent of one reported group. Some occur immediately, and others thirty to ninety minutes after the injection. They always clear within a week.

Injection of diodrast into persons allergic to the medium may produce alarming symptoms. One case reported developed immediate hemiparesis and aphasia which cleared in twenty-four hours. The petechial hemorrhages in the conjunctiva and face disappeared in five days.

One case is reported in which there was a partial loss of vision following filling of the external carotid artery only. There are rich anastomoses between branches of the external carotid and ophthalmic arteries which can account for the above phenomenon.

In 1 case reported by the authors the intracranial branches of the internal carotid arteries on both sides were filled simultaneously by injecting one carotid artery and compressing the other in the neck. The patient developed total blindness almost immediately after the injection. There was only slight narrowing of the retinal vessels. Twenty minutes after the injection a bilateral stellate block was done followed in a few minutes by return of light perception by the patient. After twenty-four hours the right homonymous fields returned, and forty-eight hours after the injection, the visual fields and acuity were again normal. The authors concluded that the blindness was due to interference with blood supply to visual pathways above the geniculate bodies. There was no retinal ischemia. They warn against

bilateral internal carotid angiography done by the above technique. They conclude that although occasional transient ocular changes may occur during carotid angiography, permanent visual loss has not been reported.

In the second part of this paper, the authors discuss in detail the ocular signs of thrombosis of the internal carotid artery including blindness of the homolateral eye; retinal hemorrhages; pain in the eye; hemianopsia; pupillary changes; ophthalmoplegia and papilledema.—*Frank M. Windrow, M.D.*

Otenasek, Frank J., and Markham, James. Transient loss of vision following cerebral arteriography. *J. Neurosurg.*, Sept., 1952, *9*, 547–550.

The authors present a case which developed partial blindness of the homolateral eye about two hours after four 15 cc. injections of diodrast (35 per cent) into the common carotid artery. The internal carotid artery did not fill and was presumably occluded. The patient developed a large central scotoma, constriction of his peripheral visual fields, which was greater on the nasal side, and marked loss of visual acuity. Fundoscopic examination was negative except for reddening of the macula. Three stellate blocks were done. All signs and symptoms were almost gone in twenty-one hours and vision was entirely normal in forty-eight hours.

Several theories as to the possible mechanism are presented, but none of them can adequately explain the visual changes. As yet there is no convincing explanation.—*Frank M. Windrow, M.D.*

Ödman, Per. Notes on the technique in phlebography of the thigh. *Acta radiol.*, Nov., 1952, *38*, 367–374.

Since September, 1951, the author has used a method which employs the same principle for retrograde phlebography by the injection of contrast medium into the common femoral vein and for phlebography by the injection of contrast medium into the popliteal vein. The vein is percutaneously punctured with a needle approximately 12 cm. in length. Through the needle a fine polyethylene catheter about twice the length of the needle and of sufficient thickness to fill the bore without permitting leakage, is introduced. The catheter is threaded on a somewhat shorter, straight steel wire (the "leader"). By this means, it is possible to direct the catheter to some extent, so that it does not become entangled within the lumen of the vein or come to rest in a lateral branch. The next step is the removal of the "leader" and the needle, while the fine polyethylene catheter remains in the vein and is then connected to a similar catheter of the desired length. The system is continuously flushed with physiologic saline solution. This arrangement affords great advantages: the patient may be examined in almost any position and the leg rotated between exposures in order that suitable projections may be obtained. The operator injecting the contrast medium may stand behind a protective lead screen during the whole investigation.

The set-up is so arranged that anteroposterior roentgenograms may be taken in rapid sequence with the Potter-Bucky diaphragm and at a constant distance. In the same manner roentgenograms may be taken with the leg rotated so that different projections are obtained.—*Mary Frances Vastine, M.D.*

Venturini, A. La flebografia per lo studio dell'insufficienza venosa cronica dell'arto inferiore. (Phlebography for the study of chronic venous insufficiency of the lower extremity.) *Ann. ital. di chir.*, Nov., 1952, *29*, 709–725.

This article includes a good discussion of the anatomy and physiology of the venous circulation of the leg in the normal and pathological cases. The various methods of visualization of the veins were used in the study of the abnormal cases in order to establish proper indications for the form of treatment to be instituted.

(1) Direct injection into the external saphenous vein: 20 cc. of 50 per cent contrast medium is injected in fifty seconds. The patient is placed in a horizontal position and elastic constricting bands are utilized at various levels, either above the ankle, at the knee or the thigh. The vein is injected percutaneously or exposed surgically under local anesthesia. The films are exposed as the last cc. of contrast medium is being injected. Later the vein is flushed with 10 cc. of normal saline solution to which 1 per cent novocain has been added.

(2) Arterial injection after exposure of the posterior tibial artery just behind the internal malleolus: 40–55 cc. of 50 per cent solution is injected in fifty seconds. Since this procedure is very painful general anesthesia is often necessary to keep the patient quiet.

(3) Transmedullary injection: this is used, either through the tibia or the calcaneal bone. A sternal puncture needle is driven through the cortex of the bone until the point lies in the medullary canal. About 20 cc. of 50 per cent contrast medium is injected in fifty seconds.

(4) Retrograde method: this consists of exposing the femoral vein under local anesthesia. Pressure on the vein proximal to the level of injection is used or the patient is placed in an upright position during the injection. Normally only 3–8 cm. of the femoral vein is visualized. If the valves are incompetent, reflux into the veins in the more dependent veins is seen.

For visualization of the femoral and iliac veins the author has used the following methods: (1) Percutaneous injection of 25–30 cc. of 50 per cent solution in five to six seconds. To diminish dilution of the contrast medium—pressure of 30–40 mm. of Hg is

applied to the opposite thigh. (2) Direct injection into the femoral vein of 20 cc. of 50 per cent opaque medium in five seconds with a constricting band below the site of injection around the thigh. (3) Catheterization with passing of the catheter as far as possible and injecting 20–25 cc. of 50 per cent solution in five seconds. (4) Injection of the dorsal vein of the penis or clitoris after surgical exposure under local anesthesia, using 20 cc. of 50 per cent solution in ten seconds. (5) Transmedullary injection, using either the pubic bone, iliac crest or greater trochanter of the femur. This usually requires general anesthesia; 1 per cent novocaine is added to the contrast medium to prevent spasm of the vein.

The author has employed all of these methods in cases of edema following phlebitis, thrombophlebitis, phlebothrombosis, thrombosis following fractures, acute arterial thrombosis and in elephantiasis. The procedure most frequently used and the one which gave the best results was the direct injection into the vein.—*Peter E. Russo, M.D.*

DIOGUARDI, NICOLA. La flebografia transmedullo-ossea. (Transmedullary phlebography.) *Ann. ital. di chir.*, Nov., 1952, *29*, 726–731.

This method of phlebography was used in those cases in which direct injection into the vein was diffi cult or hazardous as, for example, in cases of eczematosis, varices, edema and infection.

Under aseptic technique, a small skin incision is made over the bone away from joints and important soft tissue structures. A sternal puncture needle is driven into the bone and precuations are taken to be certain that the point lies in the medullary canal. A general anesthesia is usually necessary and 30–40 cc. of a 70 per cent contrast medium is injected as rapidly as possible. The film exposures are made as the last few cc. are being injected. The calcaneal bone serves the best purpose. The dangers of infection and contrast medium sensitivity are more theoretical than actual and form no contraindications to this method.—*Peter E. Russo, M.D.*

MARCOZZI, GIOVANNI. In tema di techniche e di quesiti flebografici. (On the subject of phlebography techniques and problems.) *Ann. ital. di chir.*, Nov., 1952, *29*, 732–741.

The author points out the fact that phlebography should have three features: (1) simplicity of procedure, (2) should be innocuous to the patient, and (3) should provide conclusive diagnostic results.

The simplest method is subcutaneous injection of the contrast medium in a suitable vein on the dorsum of the foot. Should this prove to be a difficult problem, transmedullary injection is used. Injection of 1 per cent novocain solution prior to the injection of the contrast medium prevents spasm of the veins to be visualized.

For the procedure to be innocuous one must avoid injecting large amounts of contrast medium or one of too high a concentration. The author uses 20 cc. of 40 per cent solution. The patient is tested for dye sensitivity—apparently he uses all three tests. After the procedure the patient is given 1 cc. or 50 mg. of heparin through a vein in the arm to prevent thrombosis of the veins of the leg.

To obtain conclusive diagnostic results a meticulous technique must be employed and careful attention given to several details. The author injects the vein with the patient in the erect position. Only one constricting band is applied just above the ankle to permit good filling of the deep veins of the leg. Although the contrast medium must be injected rapidly this should not be exaggerated. Roentgenograms in at least two views at right angles to each other or serial films should be taken about fifteen to twenty seconds after the injection has been completed.—*Peter E. Russo, M.D.*

## GENERAL

TORGERSEN, J. The triad of Kartagener; a contribution to its hereditary and developmental basis. *Schweiz. med. Wchnschr.*, July 26, 1952, *82*, 770–771.

This syndrome, which is named after the author who first described it in 1933 consists of situs inversus, bronchiectasis and nasal polyps or a chronic hyperplastic rhinitis. Two cases of nasal polyps are described in sisters thirteen and six years of age. Both showed situs inversus of the viscera. Both had symptoms of bronchitis, and the roentgenogram of the younger showed opacities in the left lower lobe as may be observed in bronchiectasis (apparently bronchography was not done).

In connection with this observation of a familial case of the triad of Kartagener, a review is given of the data and results previously published by the author regarding the hereditary basis of this syndrome. The bearing of the data on population genetics is considered. The data include information obtained from a survey of 185 families comprising 195 cases of situs inversus.—*Paul R. Dirkse, M.D.*